18th Annual Meeting, American College of Chest Physicians
Congress Hotel, Chicago, Illinois, June 5 - 8, 1952

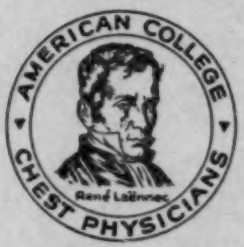
VOLUME XXI NUMBER 2

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



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DISEASES *of the* CHEST

OFFICIAL PUBLICATION

OF THE

AMERICAN COLLEGE OF CHEST PHYSICIANS

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CONTENTS:

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1. Reiser, H. G., et al.: Arch. Surg. 63: 568-575 (Oct.) 1951.

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1. J.A.M.A. 147:730-737 (Oct. 20) 1951. Literature and detailed dosage information on request.

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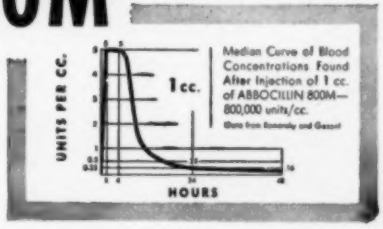

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DISEASES *of the* CHEST

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Terramycin in the Treatment of Pulmonary Tuberculosis: A Pilot Study*

LIONEL M. PFEFER, M.D.,†
FREDERIC J. HUGHES, Lt. Colonel, MC, USA and
WILLIAM E. DYE, 1st Lt., USAF (MSC)
Denver, Colorado

Introduction

Terramycin, a relatively new antibiotic with a wide range of potency, is a crystalline yellow powder obtained from cultures of the actinomycete, *Streptomyces rimosus*.[1] Its antimicrobial activity has been demonstrated against most important gram-negative and gram-positive bacteria, both aerobic and anaerobic; spirochetes, rickettsiae; and certain of the viruses.[1,2] Terramycin inhibits the growth of both streptomycin-sensitive and streptomycin-resistant strains of *Mycobacterium tuberculosis in vitro* and suppresses tuberculous infection in experimentally inoculated mice and guinea pigs.[3-6] Comparison of the antituberculous activity of Terramycin with that of other drugs indicates that Terramycin is more effective in the guinea pig than aureomycin, para-aminosalicylic acid, or amithiozone, but less effective than viomycin or streptomycin.[6]

Terramycin is readily absorbed after oral or parental administration. The serum content is maintained at a constant level for several hours after the oral administration of very small doses of Terramycin. Adequate serum levels for non-tuberculous infections may be maintained with 0.5 to 1.5 grams orally every six hours. After absorption Terramycin is concentrated in the bile. The drug is also excreted in the urine and feces in a biologically active form. Terramycin is relatively non-toxic. Doses as high as 15 grams per day have been given to individuals without sig-

*From the Chest Disease Section of the Medical Service and the Research and Development Branch, Fitzsimons Army Hospital, Denver, Colorado.
†Resident in Chest Diseases, University of Colorado School of Medicine and Fitzsimons Army Hospital.

nificant toxicity,[7] although many reports have mentioned diarrhea and slight nausea. There have been no reports in the literature to date of impairment of renal or hepatic function, depression of bone marrow, or nerve damage following the usual therapeutic doses.

Because of the demonstrated antituberculous activity and very low toxicity of Terramycin, a pilot study to determine its effectiveness in human tuberculosis was undertaken by the Veterans Administration-Army-Navy Chemotherapy in Tuberculosis Study Group. In addition to participating in this pilot study, a separate investigation was undertaken by Fitzsimons Army Hospital. This second study was designed to determine the effectiveness of Terramycin with streptomycin in view of the superiority of combinations of streptomycin and para-aminosalicylic acid over either drug alone.[8] This paper presents the experience at this hospital with Terramycin, alone and with streptomycin, in the treatment of human pulmonary tuberculosis.*

Regimens Studied and Clinical Material

The following treatment regimens were studied: (a) Terramycin hydrochloride seven grams daily in four divided doses (seven 250 milligram capsules with meals and with bedtime nourishment) for 120 days. Fifteen patients were treated by this method. (b) Streptomycin sulfate two grams intramuscularly (given in a single dose) and Terramycin hydrochloride seven grams orally (seven 250 milligram capsules given with meals and bedtime nourishment) given together every third day for 120 days. Twelve patients were treated on this program.

The 27 patients selected for the above studies had bacteriologically proved moderately or far advanced pulmonary tuberculosis, and had not received prior tuberculostatic drug therapy. In addition, five patients with chronic, far advanced fibrocaseous tuberculosis with persistently positive sputum despite all previous treatment were selected, in order to determine the time of appearance of bacterial resistance to Terramycin given alone daily. These five patients had previously received streptomycin, para-aminosalicylic acid and amithiozone therapy.

Method of Evaluation

Patients treated on both regimens were evaluated at the onset of treatment, at the mid point (60th day) during treatment, at completion of 120 days of treatment and at 60 days post treatment, in terms of clinical, bacteriologic and roentgenographic response,

*Chas. Pfizer and Company, Inc. furnished the Terramycin employed for both of these studies.

drug toxicity and bacterial resistance. All comparisons were made with reference to onset of treatment (zero day†).

Clinical evaluation included: (1) alterations of temperature, (2) variations of weight in excess of five pounds, (3) changes in sputum volume in excess of 15 milliliters and (4) cough. Patients were considered improved if there was improvement in any one of the clinical factors considered and worsening in none of the others.

Bacteriologic evaluation of the sputum was made by accepted smear and culture techniques, and of fasting gastric contents by culture alone.[9] Streptomycin sensitivity studies were performed on Herrold's Egg Yolk Agar.[10] After ten to fourteen days of incubation, growth on media containing the drug was evaluated by comparison with the control. Cultures showing growth in the ten microgram per milliliter tube equal to that in the control tube (zero micrograms per milliliter) were called resistant. Terramycin sensitivity studies were performed on solid oleic acid albumin medium[11] containing 0, 6.25, 12.5, 25, 50, 100 and 200 micrograms of the drug per milliliter. After seven days of incubation growth on the media containing the drug was evaluated by comparison with the control. Since criteria do not exist for the selection of any particular concentration of Terramycin in the presence of which growth of tubercle bacilli is indicative of a state of resistance to the drug, a concentration of 50 micrograms per milliliter, which inhibited growth in the majority of instances after 120 days of therapy, was selected as the critical concentration for this study.

Incidence and severity of toxic manifestations were determined by appropriate clinical and laboratory studies, with particular attention to detection of eighth nerve damage, gastro-intestinal toxicity, hepatic and renal insufficiency, blood dyscrasias and dermatitis.

Evaluation of Regimens Studied

Complete clinical, roentgenographic, bacteriologic and drug toxicity evaluations were made of the 15 previously untreated patients who received Terramycin alone daily, and the 12 previously untreated patients who received Terramycin and streptomycin each every third day. Bacteriologic and drug toxicity evaluations only were made of the five previously treated patients selected for study of emergence of bacterial resistance. Each case was given a clinical pathologic classification based primarily on a

†However, because all of the patients received additional treatment (temporary or permanent collapse procedures and/or further chemotherapy) during the 60 days following completion of 120 day course of Terramycin or Terramycin and streptomycin, evaluation during this period was limited to consideration of worsening only.

comparison of serial roentgenograms, with consideration of duration of disease and clinical course. As shown in Figure 1, the pattern representing the percentage of cases in each clinical pathologic group was quite different in the two regimens. The group receiving daily Terramycin was composed in the main of mixed new and old lesions, while the group receiving both streptomycin and Terramycin contained a preponderance of new mixed lesions (exudative caseous pneumonic). Because of this difference in the pathologic groups and because of the relatively small number of cases in each study, no other comparison between the two regimens has been attempted.

A) *Clinical Evaluation:* In Table I it is seen that of the 12 patients who were symptomatic at the onset of daily Terramycin

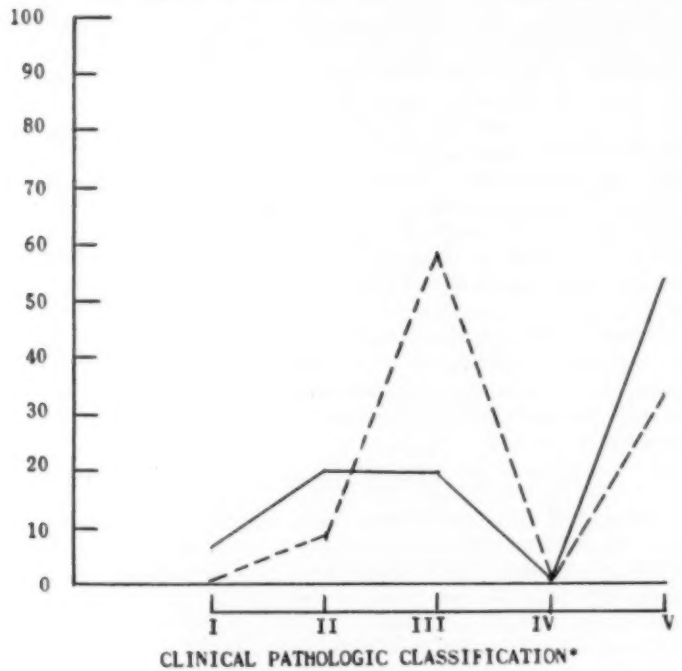

FIGURE 1

I New resolving lesions (exudative).
II New poorly resolving lesions (caseous pneumonic).
III New mixed lesions (exudative caseous pneumonic).
IV Old irreversible lesions (fibrocaseous).
V Mixed new and old lesions.

*Based chiefly on serial roentgenograms.

therapy, two became asymptomatic at 60 days and five at 120 days. Of the remaining seven symptomatic patients, at 120 days five were improved, one unchanged and only one worsened in comparison to zero day. The worsening which occurred in one case at 60 and 120 days was due to severe hemorrhage. This patient showed significant symptomatic improvement at 60 days post treatment, however, in comparison with zero day.

Of the 11 symptomatic patients receiving streptomycin and Terramycin, five became asymptomatic during treatment (Table II). The remaining six symptomatic patients showed improvement in five instances and no change in only one. During the 60 day post treatment period there were no cases which had worsening of clinical symptoms on either regimen.

TABLE I: CLINICAL EVALUATION

Fifteen patients receiving oral Terramycin, 7.0 grams daily for 120 days (Total: 840 grams).

	0 Days*	60 Days	120 Days	60 Days Post RX
Symptomatic — Improved	1	6	5	6
— Unchanged	9	3	1	1
— Worsened	2	1	1	0
TOTAL	12	10	7	7
Asymptomatic	3	5	8	8
TOTAL PATIENTS	15	15	15	15

*Improved, unchanged, and worsened at 0 day refer to trend during the preceding 60 days.

TABLE II: CLINICAL EVALUATION

Twelve patients receiving oral Terramycin 7.0 grams with intramuscular streptomycin 2.0 grams every third day for 120 days (Total: 280 grams of Terramycin and 80 grams of streptomycin).

	0 Days*	60 Days	120 Days	60 Days Post RX
Symptomatic — Improved	7	7	5	5
— Unchanged	3	1	1	1
— Worsened	1	0	0	0
TOTAL	11	8	6	6
Asymptomatic	1	4	6	6
TOTAL PATIENTS	12	12	12	12

*Improved, unchanged, and worsened at 0 day refer to trend during the preceding 60 days.

B) *Roentgenographic Evaluation:* Table III shows that roentgenographic improvement occurred promptly in the majority of cases on the daily Terramycin regimen. No instances of worsening were found at the 120 day period. It is noted that 11 of the 12 patients showing roentgenographic improvement at 120 days had already shown improvement after 60 days of drug therapy. However, cavity closure was not seen in any of the 12 cases with cavity at zero day. One patient who had improved during therapy and

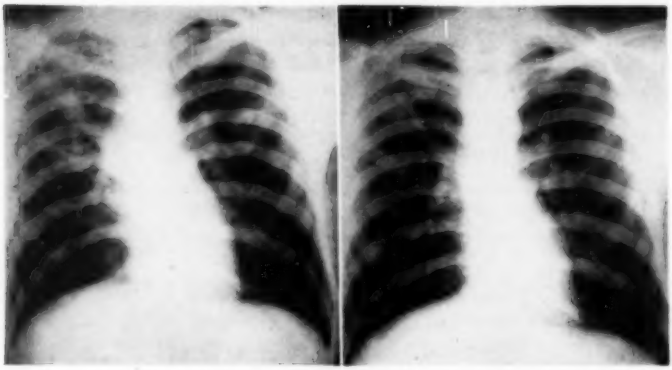

FIGURE 2a

0 Days 120 Days

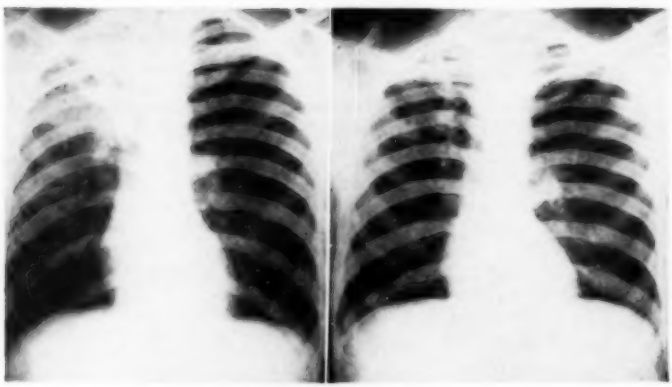

FIGURE 2b

0 Days 120 Days

Roentgenographic response of four patients showing definite regression after receiving 7.0 grams of Terramycin (oral) daily for 120 days. The film marked "0 Days" in each case was taken at the start of therapy. The film marked "120 Days" in each case was taken at completion of 120 days of therapy.

one other who remained unchanged, worsened during the 60 day follow-up period despite the initiation of pneumoperitoneum at the 120 day point. (Both have subsequently responded favorably to further drug treatment, one with streptomycin and para-amino-salicylic acid, the other with additional Terramycin.)

The zero day and 120 day roentgenograms showing definite regression of four patients who received orally 7.0 gms. Terramycin daily for that period are reproduced (Figures 2a, b, c, d). It is felt that the degree of improvement shown in these four patients exceeds that which might be expected on a rest regimen alone, and is comparable to that obtained with streptomycin.

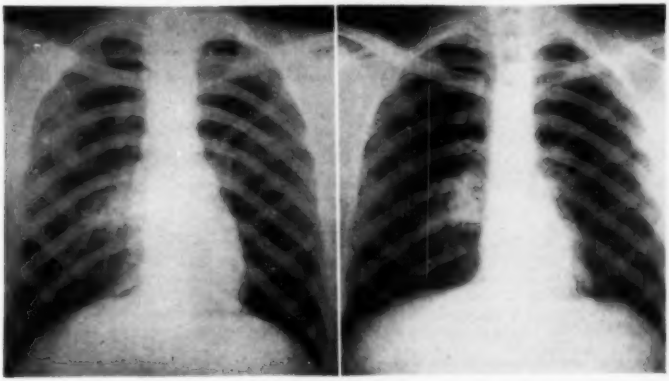

FIGURE 2c

0 Days 120 Days

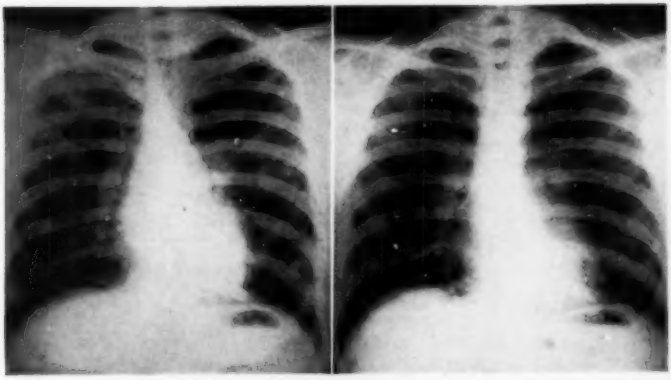

FIGURE 2d

0 Days 120 Days

In Table IV, streptomycin and Terramycin, roentgenographic improvement in 11 of the 12 cases is noted at 120 days; 10 of these had shown improvement at 60 days. All cases continued to improve at the 60 day post treatment period during which other therapy was added. Cavities present in 11 cases at the onset of therapy closed in three instances.

C) *Bacteriologic Evaluation:* The bacteriologic status of the 15 patients treated with Terramycin daily is shown in Table V. All

TABLE III: ROENTGENOGRAPHIC EVALUATION

Fifteen patients receiving oral Terramycin 7.0 grams daily for 120 days (Total: 840 grams).

	0 Days*	60 Days	120 Days	60 Days Post RX
Improved — Slight	3	5	3	2
— Moderate	0	5	7	7
— Marked	0	1	2	2
TOTAL	3	11	12	11
Unchanged	7	4	3	2
Worsened	5	0	0	2
TOTAL PATIENTS	15	15	15	15
Cavity Present	12	12	12	10

*Improved, unchanged, and worsened at 0 day refer to trend during the preceding 60 days.

TABLE IV: ROENTGENOGRAPHIC EVALUATION

Twelve patients receiving oral Terramycin 7.0 grams with intramuscular streptomycin 2.0 grams every third day for 120 days (Total: 280 grams of Terramycin and 80 grams of streptomycin).

	0 Days*	60 Days	120 Days	60 Days Post RX
Improved — Slight	3	8	6	6
— Moderate	0	2	5	5
— Marked	0	0	0	0
TOTAL	3	10	11	11
Unchanged	7	2	1	1
Worsened	2	0	0	0
TOTAL PATIENTS	12	12	12	12
Cavity Present	11	11	8	7

*Improved, unchanged, and worsened at 0 day refer to trend during the preceding 60 days.

yielded sputa positive for acid fast bacilli which were sensitive to Terramycin at start of treatment. After 120 days of therapy six yielded negative sputa, i.e., negative for at least 30 days on at least two different sputum cultures. During the 60 day post chemotherapy follow-up period an additional case became negative, so that the final status at the 60 day follow-up point was eight positive and seven negative. Thus, the majority of sputa converted to negative during chemotherapy, rather than in the follow-up period.

The Terramycin sensitivity status of patients at the 0, 60 and

TABLE V: BACTERIOLOGICAL EVALUATION

Fifteen patients receiving oral Terramycin 7.0 grams daily for 120 days (Total: 840 grams).

	0 Days	60 Days	120 Days	60 Days Post RX
Negative*	0	3	6	7
Positive — Terramycin Sensitive	15	12	8	7
— Terramycin Resistant*/	0	0	1	1
Total Positive	15	12	9	8
TOTAL PATIENTS	15	15	15	15

*Negative for at least 30 days on at least two different sputum cultures.
**Growth in presence of 50 micrograms of Terramycin per milliliter of medium equal to growth on control (0 micrograms per milliliter).

TABLE VI: BACTERIOLOGICAL EVALUATION

Twelve patients receiving oral Terramycin 7.0 grams with intramuscular streptomycin 2.0 grams every third day for 120 days (Total: 280 grams of Terramycin and 80 grams of streptomycin).

	0 Days	60 Days	120 Days	60 Days Post RX
Negative*	0	4	4	7
Positive — Sensitive to both Streptomycin and Terramycin	12	8	8	5
— Terramycin Resistant**	0	0	0	0
— Streptomycin Resistant†	0	0	0	0
Total Positive	12	8	8	5
TOTAL PATIENTS	12	12	12	12

*Negative for at least 30 days on at least two different sputum cultures.
**Growth in presence of 50 micrograms of Terramycin per milliliter of medium equal to growth on control (0 micrograms per milliliter).
†Growth in the presence of 10 micrograms of streptomycin per milliliter equal to growth on the control (0 micrograms per milliliter).

120 day periods are also reported in Table V. Near the end of therapy cultures from one patient showed a marked increase in resistance to Terramycin in vitro. A total of seven cultures which grew well on 50 but not 100 micrograms of Terramycin per milliliter have been obtained from this patient. He was a 21 year old white soldier with far advanced disease of recent duration, with a very large cavity in the right lower lobe which remained open despite drug treatment and pneumoperitoneum. This patient's sputum remained persistently positive for tubercle bacilli, and he showed very little clinical response to therapy.

Table VI shows the bacteriologic status of patients treated on the regimen employing streptomycin and Terramycin. All 12 patients had sputa positive for tubercle bacilli at the zero day period. The sputa of four patients were negative after 120 days of combined drug treatment and 60 days subsequent thereto. During the follow-up period the sputa of three additional patients became negative. Cultures from the eight patients who remained positive during and at completion of therapy were in all instances sensitive to 50 micrograms of Terramycin and to 10 micrograms of streptomycin per milliliter.* This is in striking contrast to our experience with the use of streptomycin alone every third day for 120 days wherein 31.7 per cent of the patients with positive sputa on or after completion of drug therapy yielded resistant organisms.[12] It also suggests a parallel to our experience with another form of combined therapy, namely, streptomycin every third day and para aminosalicylic acid daily, where-in no organisms resistant to either drug were encountered at completion of 120 days of therapy.[8]

The five patients studied from the standpoint of Terramycin resistance continued to yield tubercle bacilli sensitive to the drug after completion of 120 days of therapy.

D) *Drug Toxicity:* Although Terramycin is an antibiotic with almost no reported toxicity in the usual dosage range, it was felt that investigation of the possibility of its occurrence should be made because of the larger doses administered alone and in combination with streptomycin. Daily clinical observation, weekly complete blood counts and urinalyses, bromsulfalein excretion and prothrombin time determinations twice monthly for the first two months and monthly thereafter during drug administration, caloric

*The criterion used to designate resistance to streptomycin is growth equal to the control (0 micrograms per milliliter) on medium containing 10 micrograms of the drug per milliliter. The observation that cultures from these patients showed *no* growth on media containing 10 micrograms of streptomycin per milliliter offers additional evidence that the use of Terramycin as a streptomycin adjunct will delay the emergence of streptomycin resistant tubercle bacilli.

tests of vestibular function and audiograms at beginning and end of therapy showed no evidence of any toxicity to either antibiotic.

Gastro-intestinal irritation, manifested by diarrhea, nausea and occasional vomiting, was encountered in every patient on either regimen during the initial two or three weeks of drug treatment, but persisted with sufficient severity to compel withdrawal of antibiotics in only two patients. After demonstrating their inability to retain either seven or five grams of Terramycin daily, these two patients approximately two weeks later were given a trial on the regimen employing Terramycin with streptomycin, each every third day. They were likewise unable to tolerate this schedule, were therefore dropped from the series and are not included in the clinical, roentgenographic or bacteriologic evaluations reported herein. Both were then placed on our standard streptomycin (every third day)-para-aminosalicylic acid (daily) regimen.[5] One took this without difficulty while the other encountered some distress from the para-aminosalicylic acid. One other patient after two weeks of inability to tolerate daily Terramycin, was transferred to the streptomycin-Terramycin regimen which he followed without difficulty, and is included in the twelve patients evaluated on that regimen. In all instances the diarrhea was non-colicky and of slight to moderate severity (five to ten soft stools daily), without other gross alteration, or appearance of blood or mucus. Diarrhea was not accompanied by constitutional symptoms in any case.

In controlling the gastro-intestinal irritability, reassurance and continuance of the drug were considered of primary importance. Other measures employed in controlling nausea and vomiting included Dramamine, phenobarbital, atropine and rectal Nembutal. Giving the Terramycin with meals was most effective in reducing gastro-intestinal irritability. The evening dose was given with a sandwich or soup, which was preferred to the cold milk usually recommended for improving the palatability of the drug. The patients found that interspersing capsules of Terramycin with mouthfuls of food was the easiest manner of taking the drug.

Discussion

The majority of patients while under treatment with Terramycin or Terramycin and streptomycin exhibited prompt improvement clinically and roentgenographically. However, in the absence of a larger, adequately controlled study, it cannot be stated with certainty that the magnitude and promptness of response are greater than might be ascribed to a bed rest regimen alone.

Cavity closure did not occur in the 12 patients treated with Terramycin alone. When streptomycin was combined with Terra-

mycin cavities were lost to view in three of the 11 patients with cavity at zero day. This effect is similar to that obtained with combinations of streptomycin and para-aminosalicylic acid. The incidence of sputum negativity reported in this paper is lower than that obtained with larger series treated for a like period with streptomycin every third day and para-aminosalicylic acid daily[8] but appears higher than would be expected from a similar group of patients treated on bed rest alone.

More striking is the low incidence of bacterial resistance encountered in this very small series. Nine of the 15 patients who received seven grams of Terramycin daily continued to yield positive cultures after 120 days of therapy, but in only one case did the tubercle bacilli become resistant to 50 micrograms of Terramycin per milliliter. If the five patients selected for resistance study alone—all of whom had positive sputa containing Terramycin sensitive tubercle bacilli at completion of therapy—are added to the foregoing group, one notes that of 20 patients treated with daily Terramycin, 14 remained positive and that all but one of these were sensitive *in vitro* to 50 micrograms of Terramycin per milliliter. The incidence of bacterial resistance to Terramycin encountered when Terramycin was administered alone was, therefore, 5.0 per cent of the 20 patients treated.

Of the 12 patients treated with Terramycin seven grams and streptomycin two grams, each every third day, eight had positive sputa at the 120 day point. Cultures from all were sensitive to both streptomycin (ten micrograms per milliliter) and to Terramycin (50 micrograms per milliliter). Although the small number of patients allows only a tentative opinion, certain similarities to our experience with streptomycin and para-aminosalicylic acid are evident. When streptomycin alone is given every third day, the incidence of patients with organisms resistant to streptomycin after 120 days is 31.7 per cent.[12] On the other hand, when streptomycin is given every third day with para-aminosalicylic acid twelve grams daily, no organisms resistant to either drug are encountered after 120 days of such therapy.[8] When streptomycin is given every third day with para-aminosalicylic acid also every third day, for a similar period, bacterial resistance to streptomycin is encountered in 30 per cent of the patients with positive cultures at the end of therapy.[13] Thus the fact that no instances of resistance to streptomycin were observed when streptomycin was given with Terramycin, both every third day, suggests that Terramycin exerts a suppressive effect on the emergence of bacterial resistance to streptomycin similar to that exerted by para-aminosalicylic acid given daily. If these observations are confirmed in larger series of cases, Terramycin may become a valuable adjunct to

streptomycin in the treatment of tuberculosis, if only by virtue of its ability to suppress the emergence of organisms resistant to streptomycin.

CONCLUSIONS

1) To determine the efficacy of Terramycin in the treatment of pulmonary tuberculosis 32 patients with moderately or far advanced disease were treated for 120 days on either of two regimens: 20 with seven grams of Terramycin alone daily, and 12 with seven grams Terramycin combined with two grams streptomycin both every third day.

2) Varying degrees of clinical and roentgenographic improvement, but no instances of worsening, were noted.

3) Nine of the 15 patients treated with Terramycin alone continued to yield positive cultures at the end of therapy. Tubercle bacilli isolated from one of these nine patients at completion of therapy were resistant to 50 micrograms of Terramycin per milliliter. Positive cultures were obtained from eight of the 12 patients treated with both streptomycin and Terramycin. Tubercle bacilli from all eight patients remained sensitive to both chemotherapeutic agents. In view of our previous experience with streptomycin intermittently, alone or in combination with para-aminosalicylic acid daily or intermittently, this would indicate that Terramycin has a definite suppressive effect on the emergence of bacterial resistance to streptomycin when both drugs are given concomitantly.

4) While gastro-intestinal irritation was encountered in practically all instances, it was sufficiently severe to cause cessation of therapy in only two of 34 patients started on these regimens. No other evidence of toxicity was encountered.

SUMMARY

A preliminary investigation of the use of Terramycin alone and concomitantly with streptomycin in the treatment of pulmonary tuberculosis indicates that Terramycin may be valuable, particularly as an adjunctive chemotherapeutic agent, in delaying the emergence of bacterial resistance to streptomycin. Further clinical trials of Terramycin, especially in combination with streptomycin, appear warranted.

RESUMEN

Una investigación preliminar del uso de la Terramicina sola y simultáneamente con estreptomicina en el tratamiento de tuberculosis pulmonar indica que la Terramicina puede ser valiosa, especialmente como un agente quimioterapeutico adjunto, en retrasar la presentación de la resistencia bacteriana a la estreptomicina. Parece que sería justificado hacer nuevas pruebas clínicas

con la Terramicina, especialmente en combinación con la estreptomicina.

RESUME

Les auteurs rapportent leurs recherches préliminaires sur l'usage de la terramycine isolément ou associée à la streptomycine dans le traitement de la tuberculose pulmonaire. Celle-ci montrent que la terramycine peut être efficace, particulièrement comme adjuvant de la chimiothérapie, en retardant l'apparition de la résistance des bacilles à la streptomycine. Il parait opportun de tenter de nouveaux essais avec la terramycine, surtout en combinaison avec la streptomycine.

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An Evaluation of the Effect of Khellin* on the Pulmonary Circulation in Man**

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Introduction

It has recently been suggested on the basis of animal experimentation and in terms of clinical response that Khellin is a potent coronary vasodilator, relaxes bronchiolar musculature, and therefore is a useful drug in the treatment of angina of effort, bronchial asthma, and chronic cor pulmonale. We have attempted to evaluate, objectively, the effect of khellin on the pulmonary circulation and cardiac output in man by means of cardiac catheterization of a series of five patients with pulmonary hypertension associated with mitral stenosis or chronic lung disease.

Khellin, a dimethoxy-methyl-furano chromone, has been reported to be the most biologically active compound of three which have been isolated from the plant, Amni visnaga lam, which grows wild in Egypt, Arabia, and other Eastern Mediterranean countries. The drug is rapidly absorbed, uniformly distributed in all organs and tissues, slowly destroyed or excreted, and does not impair renal function. Maximum concentration is obtained in five to seven minutes when the drug is given intramuscularly, and in 10 to 15 minutes following oral administration.[1-3] In therapeutic doses, it appears to have no effect on blood pressure, heart rate, or oxygen requirement of the heart.[4] Toxic reactions which have been observed are nausea, vertigo, flushing, diarrhea, constipation, somnolence, insomnia, urticaria, and dermatitis.[1,4]

On the basis of early investigation, it appears that khellin relaxes all visceral smooth muscle in animals.[5] As compared to aminophylline khellin has been claimed to be at least four to six times more potent than the former in its ability to relax the bronchiolar musculature of perfused guinea pig lungs[3] and to increase coronary outflow in heart-lung preparations in dogs and in the isolated perfused rabbit heart.[1,3]

Oral or intramuscular administration of a single dose of 50 to 200 mg. in man increases the blood concentration above the

*The khellin used in this study was kindly provided by the Smith, Kline and French Laboratories.

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minimal effective concentration which has been shown to increase coronary outflow and relax bronchiolar musculature in animals.[3]

Clinically, Anrep[1,6] reported a good response in 140 of 250 patients treated with khellin for angina of effort, a moderate response in 85, and no response in the remaining 25. De War[7] compared Khellin with glyceryl trinitrate with regard to its ability to prevent pain in angina of effort and considered them to be comparable though the former was longer acting. Electrocardiogram changes were less marked with khellin. Abrust and Levine[8] reported clinical improvement in 60 per cent of 53 patients with angina to whom they administered khellin. However, Greiner et al.,[9] in a recent carefully controlled study of patients with angina, noted no greater clinical response to khellin than to placebos. Katz, et al.,[10] recently reported a good response in 11 of 14 patients with angina pectoris and moderate in one. He also obtained marked symptomatic improvement in all of eight cases of cor pulmonale who were treated orally, and significant response in nine of 21 patients with acute bronchial asthma to whom khellin was given intramuscularly during an attack. In contrast, Anrep[4] earlier reported complete and prolonged relief in 41 of 45 patients with acute bronchial asthma who were similarly treated.

Method

The method used was that of venous catheterization of the right side of the heart as described by Cournand.[11] Intracardiac and femoral arterial pressures, and electrocardiograms were recorded on a Brush six-channel direct writing oscillograph, and the pressures were transmitted through Statham gauges.[12] Arterial blood was obtained through an indwelling femoral arterial needle, and venous blood, from the pulmonary artery through the catheter. Blood oxygen levels were determined on the Beckman spectrophotometer according to the methods of Hickman.[13] Oxygen consumption was measured by means of an especially modified gas meter and a Pauling oxygen analyzer. Cardiac output was calculated according to the Fick principle. Blood oxygen levels and oxygen consumption were determined in duplicate. The electrocardiogram was observed throughout the procedures by means of a Sanborn cardioscan.

The base line study consisted of pulmonary and femoral arterial pressure recordings, cardiac output, stroke volume, electrocardiogram and vital capacity, following which 100 mgs. of khellin were given. Ten minutes later pulmonary arterial pressure was recorded and a second dose of 100 mgs. was given. We then recorded pressures in the pulmonary and femoral arteries intermittently over a period of 60 to 90 minutes. At the end of this time, cardiac

output was again determined. Right ventricular and right atrial pressures were recorded as the catheter was withdrawn.

In addition, one patient was given 320 mgs. of khellin by mouth, in four divided doses, every day for six days. Following this regime, the patient was restudied. We attempted similar medication on a second patient but withdrew the drug following two days administration because of severe vertigo and flushing despite lowering of the dosage. We observed no other toxic reactions in any of our five patients.

Observations

Our observations are recorded in Table I. Patient C.S. is a 44 year old white male with a 33 year history of rheumatic heart disease. Clinical findings at the time of catheterization were indicative of mitral and aortic stenosis and insufficiency and of congestive heart failure. Electrocardiogram revealed the heart to be intermediate in position and the P waves were notched in all leads. As indicated the systolic pressure in this patient's pulmonary artery was 90 mm. Hg. and the diastolic was 44 mm. Hg. before the administration of khellin. Neither was significantly lowered at any time subsequent to the administration of the drug, nor was there any remarkable effect on cardiac output, the initial output being 3040 cc., and the final 3210 cc. Also to be noted is the fact that heart rate, stroke volume, femoral arterial pressure, arterial-venous difference, and vital capacity all remained essentially unaltered. Right ventricular pressure was elevated in this patient as was right atrial pressure.

T.W. is a 46 year old white male with a 13 year history of bronchial asthma. In addition, clinical and fluoroscopic findings were consistent with chronic pulmonary emphysema and chronic cor pulmonale. Electrocardiogram revealed tall and peaked P waves in leads II, III and AVF. As indicated pulmonary arterial pressure deviated little from the base line level of 47/17, the final pressure being 50/22. Cardiac output decreased from 2470 cc. to 1770 cc. which is probably related to the decrease in heart rate observed in this patient. Femoral arterial pressure remained essentially the same as did A-V difference. We were unable to measure right ventricular pressure due to the occurrence of multiple premature contractions. Right atrial pressure was normal. Vital capacity was not determined at the conclusion of the procedure.

A.B. is a white male, age 59, on whom a left pneumonectomy had been performed two months prior to catheterization subsequent to the diagnosis of bronchogenic carcinoma. Clinically he presented physical signs of chronic pulmonary emphysema, and pulmonary hypertension.

TABLE I: A SUMMARY OF OBSERVATIONS BEFORE AND SUBSEQUENT TO ADMINISTRATION OF KHELLIN

PATIENT		TIME: Base	10′	25′	40′	55′	70′	85′	100′	6 Days
			100 MG. KHELLIN							320 MG. KHELLIN q.d.
C.S.	Pressures (mm. Hg.):									
	P.A.	90/44	85/36	81/36	84/36	84/38	—	83/39	—	—
	F.A.	117/66	121/66	116/62	120/66	123/66	—	119/64	—	—
	R.V.	—	—	—	—	—	—	75/24	—	—
	Mean R.A.	—	—	—	—	—	—	12	—	—
	Cardiac Output (c.c./min.)	3040	—	—	—	—	—	3210	—	—
	Heart Rate	81	80	82	85	80	—	83	—	—
	Stroke Volume (c.c.)	38	—	—	—	—	—	39	—	—
	A-V Difference (Vol. Pct.)	0.08	—	—	—	—	—	0.05	—	—
	Vital Capacity (Pct. of Normal)	74	—	—	—	—	—	68	—	—
T.W.	Pressures (mm. Hg.):									
	P.A.	47/17	46/18	48/18	49/22	54/22	50/22	—	—	—
	F.A.	133/77	112/77	126/70	112/63	126/70	126/77	—	—	—
	R.V.	Unable to measure			Unable to measure					
	Mean R.A.	—	—	—	—	—	0.8	—	—	—
	Cardiac Output (c.c./min.)	2470	—	—	—	—	1770	—	—	—
	Heart Rate	100	93	95	92	90	91	—	—	—
	Stroke Volume (c.c.)	25	—	—	—	—	20	—	—	—
	A-V Difference (Vol. Pct.)	5.46	—	—	—	—	5.53	—	—	—
	Vital Capacity (Pct. of Normal)	60	—	—	—	—	—	—	—	—
A.B.	Pressures (mm. Hg.):									
	P.A.	40/16	42/16	44/13	—	39/12	38/13	42/16	—	—
	F.A.	121/69	121/69	128/73	—	130/69	143/76	140/77	—	—
	R.V.	—	—	—	—	—	—	36/5	—	—
	Mean R.A.	—	—	—	—	—	—	2.0	—	—
	Cardiac Output (c.c./min.)	3295	—	—	—	—	—	3560	—	—
	Heart Rate	75	70	72	—	78	80	83	—	—
	Stroke Volume (c.c.)	44	—	—	—	—	—	43	—	—
	A-V Difference (Vol. Pct.)	5.26	—	—	—	—	—	4.9	—	—

PATIENT		TIME: Base	10′	25′	40′	55′	70′	85′	100′	6 Days
		100 MG. KHELLIN							320 MG. KHELLIN q.d.	
S.C.	Pressures (mm. Hg.):									
	P.A.	24/13	25/14	24/13	27/12	—	25/12	—	—	—
	F.A.	114/65	111/60	121/70	116/70	—	119/72	—	—	—
	R.V.	—	—	—	—	—	26/4	—	—	—
	Mean R.A.	—	—	—	—	—	2.5	—	—	—
	Cardiac Output (c.c./min.)	5320	—	—	—	—	4930	—	—	—
	Stroke Volume (c.c.)	67	—	—	—	—	62	—	—	—
	A-V Difference (Vol. Pct.)	5.17	—	—	—	—	5.45	—	—	—
	Heart Rate	79	82	85	81	—	80	—	—	—
	Vital Capacity (Pct. of Normal)	63	—	—	—	—	65	—	—	—
J.C.	Pressures (mm. Hg.):									
	P.A.	37/16	34/15	35/14	38/16	35/13	33/14	—	35/16	37/19
	F.A.	121/61	111/56	126/67	113/58	116/56	125/67	—	—	123/66
	R.V.	—	—	—	—	—	—	—	30/4	34/4
	Mean R.A.	—	—	—	—	—	—	—	1.2	2.0
	Cardiac Output (c.c./min.)	4310	—	—	—	—	—	—	3800	3760
	Heart Rate	88	89	90	85	80	80	—	80	75
	Stroke Volume (c.c.)	49	—	—	—	—	—	—	48	50
	A-V Difference (Vol. Pct.)	5.7	—	—	—	—	—	—	6.02	6.11
	Vital Capacity (Pct. of Normal)	42	—	—	—	—	—	—	40	48

P.A. — Pulmonary Arterial Pressure. F.A. — Femoral Arterial Pressure.

R.V. — Right Ventricular Pressure. R.A. — Right Atrial Pressure.

A-V Difference — Arterial-Venous Difference.

Electrocardiogram revealed left axis deviation. The initial pulmonary arterial pressure was 40/16 mg. Hg. and the final pressure was 42/16, being almost constant throughout the procedure. Cardiac output remained essentially unaltered. We noted a gradual increase of 19 mm. Hg. in the systolic pressure in this patient's femoral arterial tracings, but the diastolic elevation was not as marked. Heart rate, stroke volume, and the A-V difference were constant. Right ventricular pressure was moderately elevated and right atrial pressure was normal. Vital capacity was not determined.

S.C. is a white male, 38 years of age. Clinical and x-ray findings were consistent with bronchiectasis and cor pulmonale. At the time of catheterization the electrocardiogram revealed tall and peaked P waves in leads II, III and AVF. The systolic pressure in the pulmonary artery, however, was normal being 24, but the diastolic pressure was elevated to 13 mm. Hg. and was not lowered following administration of khellin. The initial cardiac output was 5320 cc. and the final was 4930 cc. As noted, heart rate, stroke volume, A-V difference and vital capacity remained unaltered.

J.C. is a 67 year old white male with a 39 year history of bronchial asthma and additional clinical and fluoroscopic findings indicative of chronic pulmonary emphysema and cor pulmonale. Electrocardiogram revealed right axis deviation and prominent P waves in leads II, III and AVF. The initial pulmonary arterial pressure of 37/16 remained essentially the same following the intramuscular injection of khellin. This patient was given 320 mg. of oral khellin daily for six days, as previously described, and restudied. As noted here, pulmonary arterial pressure was not effected, nor was cardiac output, heart rate, stroke volume, A-V difference, systemic pressure or vital capacity.

Discussion and Conclusion

Elevation of pulmonary arterial pressure is a constant and significant factor in bronchial asthma and cor pulmonale. It has been shown by Dexter[14] and confirmed by Zimmerman[15] that the elevation in pulmonary pressure in the latter is due to pulmonary arteriolar constriction and pulmonary capillary pressure is normal. Thus to be effective in the treatment of cor pulmonale, a drug should have a pulmonary arteriolar vasodilating effect resulting in a decrease in pulmonary resistance and hence a reduction in pulmonary arterial pressure. For obvious reasons, a pulmonary vasodilating effect would also be desirable in cases of pulmonary embolism, in patients undergoing pneumonectomy, and in mitral stenosis.

In the treatment of bronchial asthma, the therapeutic aim is to relieve the bronchiolar spasm with concommitant diminution

of the elevated pressure in the alveolar sacs. With this accomplished, the pressure change is transmitted to the pulmonary capillaries and arterioles with a resultant decrease in pulmonary arterial pressure, unless as has been observed with epinephrine, the drug in addition has an arteriolar vasoconstricting effect tending to maintain or increase peripheral resistance. However, this would entail a rise in systemic blood pressure, heart rate and cardiac output.

Our data indicates that as has been previously claimed, khellin has no remarkable effect on systemic blood pressure or on heart rate. In addition, we were unable to demonstrate a significant change in pulmonary arterial pressure or in cardiac output with either intramuscular or oral use of the drug. In contrast Zimmerman[15] has demonstrated an immediate and a marked decrease of pulmonary arterial pressure and an increase of cardiac output following the administration of aminophylline to a large group of patients with pulmonary hypertension associated with a variety of etiological factors. He has shown that aminophylline not only relieves bronchiolar spasm in man, but also has a marked pulmonary vasodilating effect.

In conclusion, therefore, our observations in man, give no indication that khellin is of therapeutic value in the treatment of asthma and cor pulmonale, and are directly opposed to the claims that khellin is four times as potent as aminophylline as has been suggested by its ability to relax the bronchiolar musculature of guinea pigs and to increase coronary outflow in heart-lung preparations in dogs and in the isolated perfused rabbit heart.

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SUMMARY

1) The effect of khellin on the pulmonary circulation and on cardiac output has been evaluated in five patients with pulmonary hypertension by means of cardiac catheterization. Intracardiac and femoral arterial pressures were recorded and cardiac output and stroke volume were determined before and subsequent to the administration of khellin.

2) Five patients received 200 mg. of khellin intramuscularly, and one of these five was subsequently maintained on oral khellin for six days and recatheterized.

3) No significant alteration from base line studies was noted in pulmonary arterial pressure or in cardiac output.

4) The therapeutic usefulness of khellin in the treatment of chronic cor pulmonale and bronchial asthma is doubtful.

RESUMEN

1) Por medio del cateterismo cardiaco se ha evaluado el efecto del kelín en la circulación pulmonar y en el rendimiento cardiaco, en cinco enfermos con hipertensión pulmonar. Las presiones intracardiacas y femorales arteriales se registran y el rendimiento cardiaco y débito se determinaron antes y después de la administración del kelín.

2) Cinco enfermos recibieron 200 mg. de kelín intramuscular y uno de estos cinco fué tratado después con kelín oral por seis días entonces fué vuelto a cateterizar.

3) No hubo alteración significativa de los estudios básicos en lo referente a presión arterial pulmonar o en rendimiento cardiaco.

4) El valor terapéutico del kelín en el cor pulmonar crónico y en el asma bronquial es dudoso.

RESUME

1) L'effet de la "khelline" sur la circulation pulmonaire et le rendement cardiaque a été évalué sur cinq malades avec hypertension pulmonaire grâce au cathétérisme cardiaque. Les pressions intracardiaques et fémorales ont été notées; l'activité et le débit cardiaques furent déterminés avant et après l'administration de "khelline."

2) Cinq malades recurent 200 mg. de "khelline" par voie intramusculaire. Un d'entre eux fut maintenu ensuite à la "khelline" par voie buccale pendant six jours. Puis un nouveau cathétérisme fut exécuté.

3) Aucune modification significative ne fût notée dans la pression artérielle pulmonaire ou le rendement cardiaque.

4) L'utilité thérapeutique de la "khelline" dans le traitement du coeur pulmonaire chronique et de l'asthme bronchique est douteuse.

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Developmental Origin of Cystic, Bronchiectatic and Emphysematous Changes in the Lungs. A New Concept*

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The nature, pathogenesis and evolution of the above chronic pulmonary conditions, their frequent association, and their relationship to other pulmonary diseases are still largely open questions. These we believe can be answered logically in the light of our concept which implies that disturbances in the postnatal development of the lungs play the most important role in their origin.

Four considerations have led us to this conclusion:

1) Recent disclosures as to the course of postnatal lung development and its clinical implications.
2) Recent clinical and pathological observations of pulmonary defects associated with systemic disorders, especially metabolic disturbances of early life.
3) Clinical and pathological evidence of the frequent association of cystic, bronchiectatic and emphysematous lung changes.
4) The trend toward acceptance of "developmental factors" in the current concept of cysts, bronchiectases and emphysema, yet held to be acquired in origin.

1. *The new knowledge of postnatal lung development:* Recent disclosures have added much information as to the development of the lungs to completely change the old accepted teaching. Until quite recently the old view of Koelicker prevailed, namely, that infants are born with lungs completely formed, and that as the child grows the lungs' structures grow in size but no new elements are produced. However it is now a known fact that the lungs of the adolescent child represent the result of continued postnatal development of the organ, implying growth of new structures as well as of growth in size.

Broman[1] was first to postulate on the basis of anatomical studies that "the lungs of newborn infants are not miniatures of adult lungs," that childrens' lungs continue to grow after birth.

Willson[2] followed these with a vast amount of painstaking work

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actually demonstrating growth of new lung units in growing children. From his investigations he was led to the conclusion that "postnatal lung development" continues at least until the age of seven and in some instances to the age of 14.

Bremer[3] followed then with significant contributions which firmly established the fact that the lung does not grow by increase in size of the lobules but by increase in their number.

Most recently Engel[4] devoted a whole monograph to the subject of "The child's lung." In this he not only assembled and analyzed the new knowledge but added significant contributions of his own. He also attempted to apply this newer knowledge to the clinical and pathological aspects of diseases of children.

Clinical implications of postnatal lung development have been little considered because the knowledge is too recent and too little appreciated. We believe ours is the only effort to apply the newer knowledge to the problems to be discussed here. Engel[4] recently sought to apply it to the particular problems of pulmonary childhood diseases. However he gives scant consideration to the effects of childhood diseases in general upon the postnatal development of the lungs. Instead he concerned himself with the impact of postnatal lung development upon childhood pulmonary diseases and attributed to the latter, the age-conditioned differences in localization and character of childhood pneumonic and tuberculous infections. He dealt extensively with these clinical implications of postnatal lung development but hardly at all on their relationship to cystic and bronchiectatic conditions. These he described as congenital in origin.

The newer knowledge of postnatal lung development naturally found application in explaining the pathogenesis of pulmonary diseases in general, and of those of early life in particular. Already Willson suggested that postnatal development of the lung might be expected to play an important role in the origin of pulmonary affections. He established the fact that great individual differences exist in the pace at which children grow out of their infantile lung period, and he interpreted these differences as due to individual constitutional factors. Subsequent studies have confirmed the role of individual and racial (presumably constitutional) factors in postnatal lung development.

The first real attempt to apply the new knowledge to clinical problems in pulmonary diseases was made in 1935 in a publication[5] in which one of us collaborated. Explanation of cystic and bronchiectatic lung changes was the outstanding problem. These were then mostly considered congenital in origin, although they did occur rather too frequently to be looked upon as mere congenital anomalies. Also an increasing amount of clinical observation re-

vealed many cystic and bronchiectatic lungs definitely acquired which did not differ from those considered congenital. Belief in their congenital nature is still based chiefly on two facts:

1) They are often present in early life.

2) Their features obviously suggest disturbed development.

With increasing findings of acquired cysts, bronchiectases and emphysema and their combinations, there arose the need for a new concept to reconcile the "developmental" and yet acquired nature of the pulmonary changes. It seemed logical to apply to this the new knowledge of postnatal lung development. This led to our present concept which we have further elaborated upon in several recent publications.[6,7] In its present broad aspects it applies at all ages to these pulmonary conditions and not only to childhood.

"Disturbed postnatal lung development" is emphasized as the core of the problem. Previously we have emphasized various diseases of infancy and childhood affecting the normal growth of the lungs. Since then our observations and those of others have served to confirm the concept that cystic, bronchiectatic and emphysematous changes of "developmental" origin are acquired during infancy and childhood as a result of diseases disturbing the postnatal development of the organ. Judging by the trend in recent literature, this concept is now favored by many. Increasing numbers of recent reports associate pulmonary defects with systemic diseases of childhood, and the frequent combination of cystic and bronchiectatic changes are revealed in such pulmonary conditions.

2. *Pulmonary defects associated with diseases of childhood.* In recent years an increasing number of reports have been made on cystic and bronchiectatic lung changes associated with certain diseases either characteristic of childhood or beginning in childhood and continuing into adult life. These diseases may be divided into two groups:

(a) conditions identified with disturbances in glandular function, namely, achylia pancreatica (fibrocystic-pancreatic disease), hepatic-biliary and pituitary insufficiency, etc.,

(b) affections of the reticulo-endothelial and connective tissue systems,namely, Xanthomatosis, lipoidgranulomatosis, reticuloendotheliosis, tuberous sclerosis, scleroderma, etc.

Fibrocystic pancreatic disease representing the first group is characteristically a not uncommon disease of childhood. It begins in early childhood but even in the clinically marked cases the patients may survive into adolescent age. The clinically mild cases usually recover. Many subclinical cases exist which go unrecognized.

A most recent review[8] describes the pulmonary manifestations during life as "irregularly emphysematous lungs with areas of

atelectasis, bronchiectasis and bronchiectatic abscesses." The pathologic specimens too show bronchial dilatation and alveolar ectasia (emphysema) mostly with signs of active infection or peribronchial and perivascular fibrosis. Histologic evidence points to metaplasia of the bronchiolar lining and increased mucus secretion as a factor in the pulmonary complications. It is now recognized that the pancreatic and pulmonary manifestations are part of a systemic affection of obscure nature. Farber[9] recently suggested the name of "muco-viscidosis" to signify that the affection involves a disturbance in the mucus-secreting glands of the viscera. Ayers[10] et al., proposed that the disease involves a disturbance in the autonomic nervous regulation of visceral functions. Sympathetic denervation of the pancreas has in a number of cases resulted in improvement of the pulmonary symptoms.

In the second group, namely, Xanthomatosis, tuberous sclerosis, scleroderma, etc., cystic lung changes have been reported in increasing number. Under the descriptive title of "honeycomb lungs" Oswald and Parkinson,[11] have just reviewed the recent literature and presented 16 personally observed cases. "Six of these were associated with a general medical disorder, namely, Xanthomatosis, tuberous sclerosis and allied disorders. In the remaining 10 cases the honeycomb structure occurred as an isolated manifestation of uncertain etiology." Very significant is their observation that the cystic lung changes are identical in character regardless of whether an associated systemic disorder is demonstrable or not. They infer that a mechanical factor operates on a diseased lung.

All lungs showed extensive interstitial fibrosis, but there was no evidence as to the cause. They believed it was possible that some cases were examples of a healed general disorder.

Since the existence of these conditions has become more widely recognized, the number of reports of children so affected has increased very rapidly.[12-17] It is apparent that the clinical cases are far more frequent than previously suspected. Perhaps also an even larger proportion of subclinical conditions exists leading to developmental defects in the lungs. These remain potential cases for clinical disease becoming manifest later in life. The large number of cases turning up in later life could thus be accounted for.

It is logical to assume that the literature reflects only the most marked instances; less marked forms occur more frequently than generally realized in children who overcome milder metabolic difficulties of early life. Though temporary, these if occurring in a critical period of postnatal lung development will have an effect and result in lesser pulmonary defects which remain permanent. We believe these lesser pulmonary defects which persist may become the predisposing factors for development of cystic and bron-

chiectatic changes by inviting repeated infections acquired in later life.

3. *The association of cysts, bronchiectases and emphysema.* Clinical experience has amply proved a practically inseparable link in this triad. With most pulmonary cysts, there is combined some bronchiectasis and emphysema. In bronchiectasis, a variable degree of emphysema usually exists; and in emphysema some cystic and bronchiectatic changes are often present. The three conditions are often so intimately associated to lead to confusion in terminology. In recent literature there are numerous reports of such clinical entities as cystic bronchiectasis, cystic emphysema, bronchiectatic emphysema, etc., which obviously represent transitions between and combinations of the three conditions. Clinical observations have also amply shown that this triad makes for a chronic progressive pulmonary disease which is brought along from childhood and is carried for a variable length of time into later life.

Koontz[18] in 1925 presented the first review of "congenital cysts of the lungs" and pointed out their frequent association with bronchiectasis and emphysema. The link between the three conditions became closer in recent studies with increasing recognition of their acquired origin. It finds expression in clinical and pathological classifications which are based on actual observations of the development of cysts, bronchiectases, emphysema and their combinations as sequelae of acute and chronic pneumonitic and bronchitic inflammatory processes involving the interstitial as well as the bronchial structures.[19]

Combinations of cystic, bronchiectatic and emphysematous changes are characteristic also of the pulmonary complications of the systemic disorders discussed above. In cystic pancreatic fibrosis, bronchiectases predominate but emphysematous and cystic changes are frequent.[8,9,11,12,14] In tuberous sclerosis, Xanthomatosis, etc., the cystic and emphysematous changes are conspicuous. In scleroderma the pulmonary lesions have been described variably as cystic[15] or as bronchiolectatic and emphysematous.[13]

Clinical and pathological observations clearly indicate such close relationship between cysts, bronchiectases and emphysema which can be explained only by a common clinicopathologic process underlying their origin and pathogenesis.

The trend in current concepts: In the past 25 years there has accumulated a very extensive literature on the subject. From this it became apparent that:

1) Cystic changes in the lungs occur far more frequently than can be accounted for by congenital anomalies.
2) Cystic changes in the lungs were observed in previously nor-

mal lungs in an increasing number of cases when long range observation with the aid of x-ray could be made.

3) Cystic lung changes are often combined with bronchiectatic and emphysematous changes which are obviously acquired.

It is obvious even from a cursory review of the literature that arguments over the concepts of congenital and acquired origin still go on. Even most recent texts express strong beliefs in the congenital origin of cysts and some bronchiectases. However the idea of acquired origin is in the ascendancy. Indeed there is a notable trend to look upon most lung cysts simply as sequelae of bronchitis and bronchopneumonic processes.[20-23] This concept is expressed with emphasis in a classification frequently quoted in recent literature[19] listing the following forms: "True congenital cysts" noting that these are rare, "Chronic interstitial pneumonitis with emphysema," "Chronic bullous emphysema," "Cystic bronchiectases," "Pneumatoceles." All these are included under the heading of cystic lungs.

Even a cursory review of the literature convinces one that confusion is great. We believe that this is due to:

1) Unawareness about the facts of postnatal lung development.
2) Our inability to separate cystic from bronchiectatic and emphysematous changes because of their frequent combination.
3) The difficulty of tracing these lesions back to their origins even when long range x-ray observations are available.

It is because of these difficulties that most classifications offered in the literature are inadequate. Those maintaining congenital origin fail to account for the obviously acquired changes. The adherents of the acquired origin cannot explain their large groups merely as bronchitic and bronchopneumonic sequelae. Most of these conditions when first discovered do not appear as diseases but rather as structural defects bearing unmistakable features of maldevelopmental origin. After the publication of 1935 which was referred to above, the "developmental" theory found favor with many authors only to be confused again with the congenital concept. The term "developmental" began to be used interchangeably with the term "congenital." Thus confusion is created by misinterpretation of the term "developmental" which some workers[24] applied to the idea of maldevelopment due to congenital hypoplasia of the pulmonary structures. The implication here is that congenital hypoplasia of the lungs may eventually lead to cystic distention of these airspaces as the child grows up. It was pointed out already by Lehr[25] that cystic lungs are essentially of the nature of bullous emphysema developing in a hypoplastic lung on the basis of hypoplasia of congenital origin.

The concept that cystic changes are acquired on the basis of

pulmonary hypoplasia of congenital origin found strong support in the writings of Engel.[4] This is all the more surprising since this worker contributed much to our knowledge of postnatal development of the lungs. Engel includes cysts in the "comprehensive conception of bronchiectases" and conceives of "congenital bronchomalacia" as the special predisposing factor in their development. From his definition it is obvious that he believes in congenital hypoplasia as the basis upon which cysts and bronchiectases develop in the lungs. In the light of our knowledge of postnatal lung development and the potentialities for the occurrence of postnatal hypoplasia it would seem far fetched to insist on congenital hypoplasia.

To us it seemed more logical to assume that postnatal hypoplasia leading to a deficiency of bronchioles and alveoli may lead to cystic, bronchiectatic or emphysematous changes as the child grows up, and as its chest increases in size and power of expansion. The difference between our concept and the one just discussed lies essentially only in shifting the occurrence of hypoplasia from the prenatal to the postnatal period. As related above, recent observations have since revealed a number of systemic diseases of childhood which lead to cystic and bronchiectatic changes in the lungs. The development of these on the basis of postnatal hypoplasia appears to be a most reasonable assumption. The concept of postnatal hypoplasia has been borne out by the recent observations discussed above.

From the viewpoint of the radiologists who are discovering an ever increasing number of these pulmonary conditions, Pugh[24] recently reviewed the literature. He aptly summed up its present status in the following conclusions which best illustrate the current trend of thought on this subject:

a. In many cases of pulmonary cysts the pathogenesis cannot be definitely determined.
b. Some pulmonary cysts are congenital in origin.
c. Some pulmonary cysts may be best regarded as "developmental" in origin.
d. Some pulmonary cysts are acquired, usually as a result of pulmonary infection.
e. At times acquired factors probably cause the development of pulmonary cysts by distorting developmental processes.
f. Lesions that may not actually be pulmonary cysts may at times be distinguished with difficulty. This applies especially to emphysema and bronchiectasis.

If the term "developmental" in the above conclusions is so interpreted as to imply "postnatal development" then we have

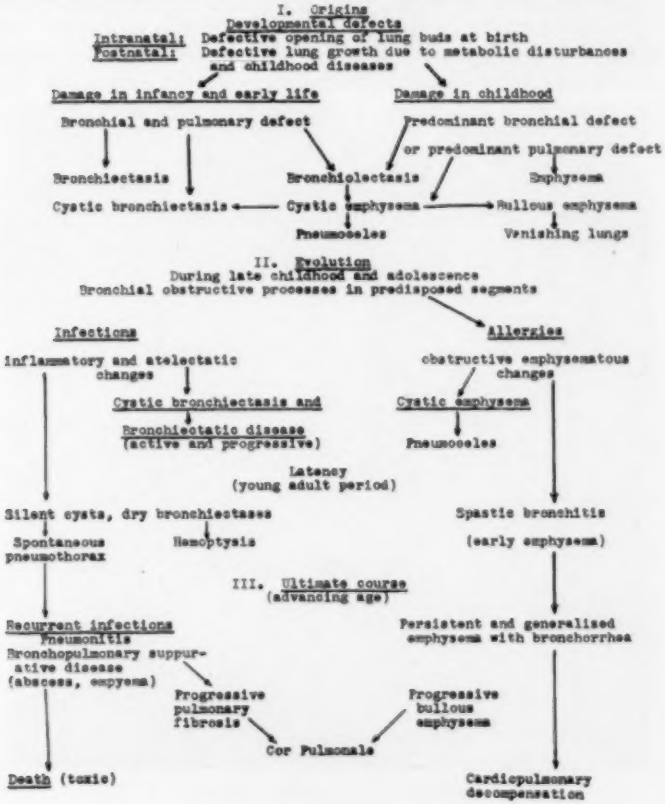
actually arrived at the concept which is promulgated in this presentation.

Our concept: In the light of the foregoing we may now state our concept of the origin of cystic, bronchiectatic and emphysematous changes in the lungs and discuss its clinical implications.

The lung at birth consists largely of the central bronchial branches and their supporting interstitial framework carrying the rich blood and lymph vessels. These bronchi terminate in the lung buds from which the first alveoli are formed by distention, as the infant begins to breathe. Postnatal development consists of continued branching of the peripheral ends of the infantile

TABLE

Natural history of bronchiectatic, cystic and emphysematous lungs



bronchial tree. Peripheral bronchioles pass inward to become major bronchi and original alveoli become bronchiolar branches. The adult alveoli represent new growth of lung tissue by a process of repeated branching, i.e., the postnatal development of the lungs during childhood years.

Defective postnatal lung development is regularly observed in children suffering from conditions affecting their metabolism during early life, as described above.

The exact nature of the developmental deficiency in all these conditions is a matter of conjecture. We may be dealing with a true hypoplasia, i.e., deficiency and resulting weakness of the structural elements themselves or with a dysfunction of the autonomic nervous regulation, resulting in disturbances of the blood supply and of the myoelastic bronchial function. Both of these will predispose to development of the characteristic lung changes during early life. It is our belief that the literature reflects only the most marked instances of these, that less marked forms of the

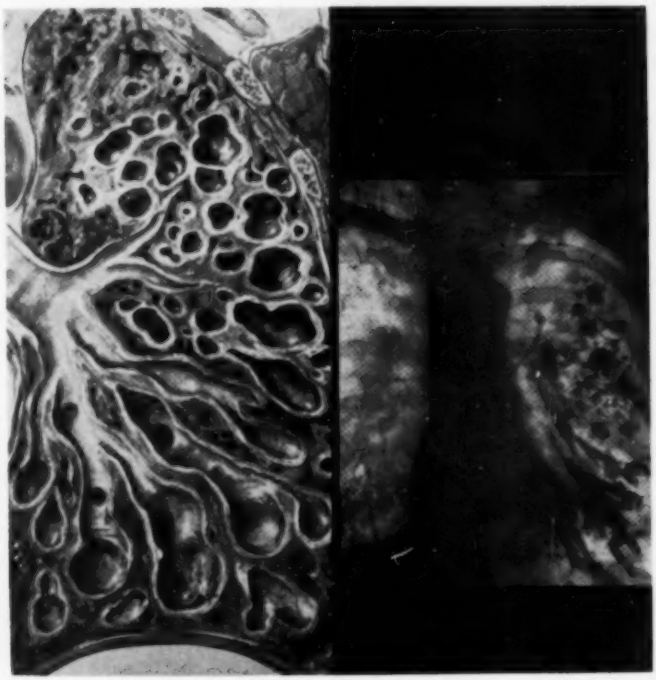


FIGURE 1: Bronchiectatic disease.

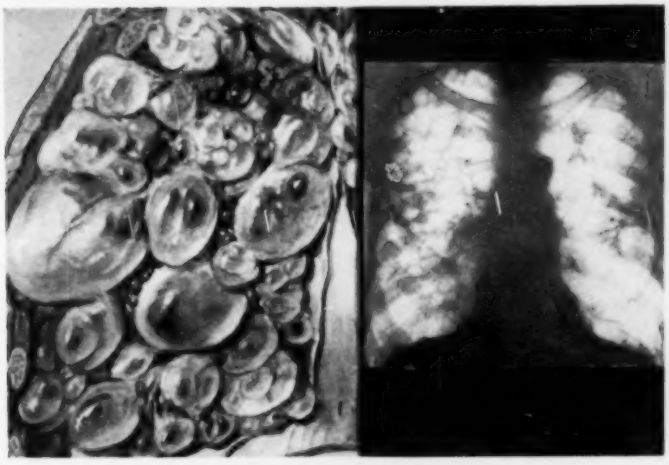


FIGURE 2: Cystic disease.

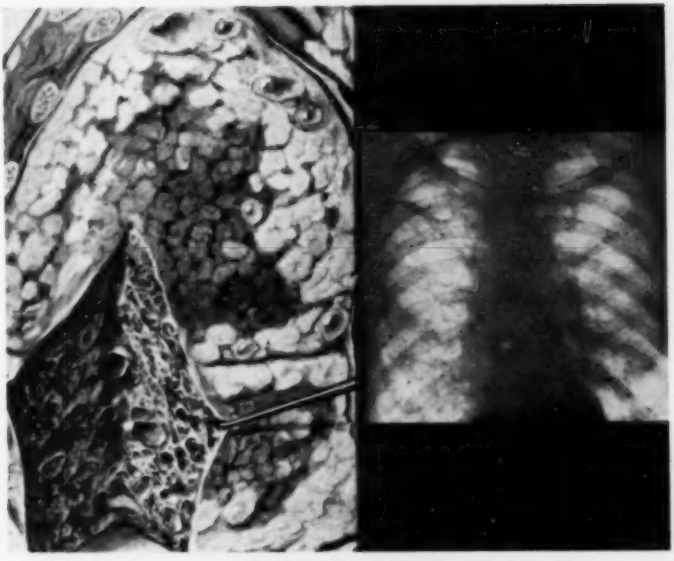


FIGURE 3: Emphysema.

Figures 1, 2 and 3, taken from the Netter collection are shown here in this sequence to illustrate the relationship indicated in text.

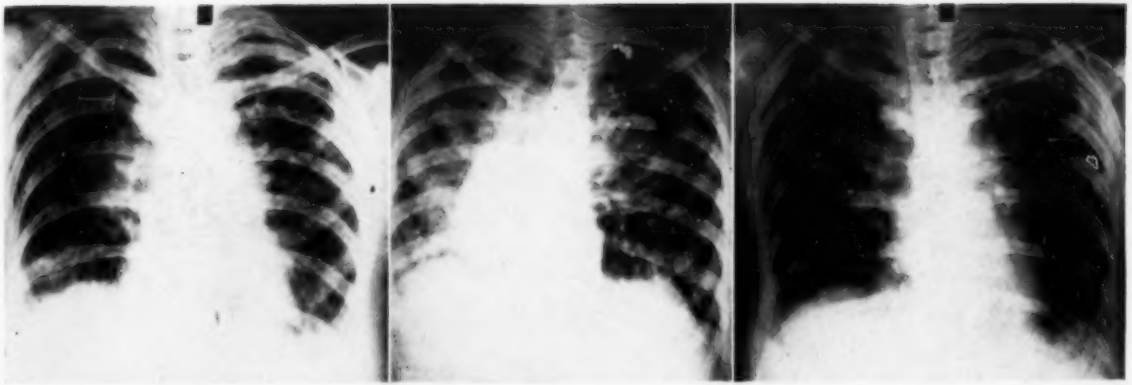


FIGURE 6 FIGURE 7 FIGURE 8

Figure 6: Pneumatoceles.—*Figure 7:* Diffuse cystic disease of the lungs in a girl of 14, first revealed by spontaneous pneumothorax. Tuberous sclerosis found subsequently.—*Figure 8:* Diffuse cystic disease of the lungs in a woman of 43. First revealed by hemoptysis 10 years ago. Spontaneous pneumothorax developed recently. Origin unknown.

same conditions are more frequent than is generally realized, in children who eventually overcome their metabolic difficulties of a milder nature. These, we believe, account for lesser pulmonary defects which persist and become the predisposing factors for development of cystic and bronchiectatic changes in *later life*.

The *type of lesion produced* depends on the *nature* and *severity* of the affection as well as the *period* of lung development at which they occur. From available evidence it can be inferred that *the earlier* the injury occurs in infancy or the more severe it is, the more likely will it affect the bronchi as well as the lungs. The result will be defects predisposing to development of cystic bronchiectasis or large lung cysts. Injuries of milder nature or those occurring during later childhood, are most likely to affect only certain segments of the bronchial tree. Such defects will predispose to development of bronchiectatic disease when more central bronchi have been affected or to development of small cysts and emphysema when peripheral bronchioles and airsacs have been injured.

The natural history of this clinicopathologic process, as we conceive it, is shown in the tabulation (Table I).

As indicated by our scheme of *origins*, bronchiectasis is on one end, and emphysema on the other. The links between them are cystic bronchiectasis and cystic emphysema. (See Figures 1, 2, 3).

Our scheme of the *evolution* indicates that the sequelae of developmental defects are determined chiefly by *mechanical obstructions* in the bronchi produced by two distinct processes, namely, *infections or allergies*, and their combinations. *Cystic or*

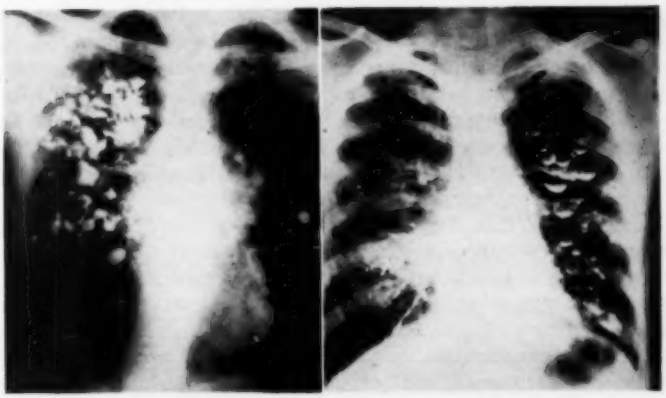


FIGURE 4 FIGURE 5

Combinations of cystic and bronchiectatic disease with emphysema.

bronchiectatic lesions predispose their bearers to *infections* which in turn bring about active bronchiectatic and cystic disease. *Bronchiolar defects* predispose allergic bearers to respiratory tract *allergies*. The fixation of allergic reactions to the respiratory tract is presumably favored by disturbed vagosympathetic nervous function in such developmental defects.

Infections and their inflammatory products are mostly associated with bronchial obstructions leading to *atelectatic* changes which are more prone to persist in *basal* portions of the lungs. Allergic *bronchospastic* states are mostly associated with *obstructive emphysema* which is more prone to persist in *upper lung* segments. The former account for progressive cystic and bronchiectatic disease. The latter explain such developments as giant cysts and pneumoceles. (See Figures 4, 5 and 6).

The mildest forms of infection result in silent lung cysts and dry bronchiectasis which may remain latent over long periods during adult life and reveal themselves only by an attack of spontaneous pneumothorax or a sudden unexplained hemoptysis. (See Figures 7 and 8).

The mildest forms of respiratory tract allergies may also remain latent over long periods and eventually manifest themselves in chronic spastic bronchitis.

These conditions are often borne even without manifestations of clinical significance until late in adult life, but eventually after a period of years or even decades, the process starts on its ultimate course. Its nature is then determined by whether infection or emphysema predominates. Infections lead to extensive bronchopulmonary suppurative disease with complicating chronic abscesses, empyemas, etc. Predominance of emphysema leads to ultimate cardiopulmonary decompensation. Their combinations are frequent; and as such, recurrent pneumonitis and progressive pulmonary fibrosis will enhance the progression of emphysema.

The *clinical picture sequence* corresponding to the above described pathogenesis is commonly seen in practice as follows:

In *childhood and adolescence* we see a range of conditions fluctuating between cases of *mild chronic protracted bronchiolitis or bronchitis* and cases of frank *bronchiectatic disease* including the severe forms of *cystic or saccular bronchiectases*.

In the young adult period, cysts, bullous structures, or dry bronchiectatic lesions are mainly clinically latent. They are often discovered by a chance x-ray. During this period allergies leading to attacks of protracted asthma like "spastic bronchitis" are a common occurrence in bearers of bronchiolar defects. (With these, bronchorrhea is as characteristic of irritable bronchioles as mucous colitis is of spastic colon).

In *middle adult life* the final clinical picture occurs, in which either infections or emphysematous processes predominate. Combinations of these are frequent, giving the composite clinical picture of chronic pulmonary disease produced by the parellel progress of recurring pneumonitis with bronchiectases, pulmonary fibroses and emphysema.

The *end* may not come until late in life with the advent of congestive heart failure of the *cor pulmonale* type.

SUMMARY

A new concept has been presented of the natural history of cystic lungs, bronchiectases and emphysema. Their origin has been traced to postnatal developmental defects. The pathogenesis of their association has been explained. The course of chronic pulmonary disease produced by the evolution of their variable combinations has been outlined.

RESUMEN

Se presenta un nuevo concepto de la génesis de los pulmones quísticos, la bronquiectasia y el enfisema. La patogenia de su asociación se explica y su origen se hace emanar de defectos de desarrollo postnatal. La evolución de las enfermedades crónicas producidas por la marcha de sus varias combinaciones se describe.

RESUME

Les auteurs présentent une nouvelle conception de la question des kystes du poumon, des bronchiectasies et de l'emphysème. Ils attribuent leur origine à des défauts du développement postnatal. Ils expliqnent une pathogénie de leur association et ils esquissent l'aspect des affections pulmonaires chroniques réalisées par l'évolution de leurs différentes combinaisons.

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The Long Range Effect of Antibacterial Therapy on Pneumonia, Empyema, Bronchiectasis and Pulmonary Abscess

(An Analysis of Incidence and Mortality in 74,489 Admissions to a Children's Hospital* in Twenty Years)

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Among the diseases that have been the victims of the newer methods of antibacterial therapy none has yielded more ground than pneumonia. The statistics over the period 1928-1949 as published, for instance, by the Metropolitan Life Insurance Company bear out the fact that "the marked decline in the death rate from pneumonia and influenza in the past quarter of a century ranks among the outstanding achievements of medical science."

In considering the epidemiological changes of a certain group of diseases over a longer period of years, one may note spontaneous or intrinsic fluctuations in the incidence of infection as well as fluctuations in the severity or virulence of the pathogenic organisms. The combination of these two factors used to be termed "genius epidemicus," which means the changing pattern of the same clinical entity.

In the case of pneumonia, of course, there also has been a succession of extrinsic or therapeutic factors which have little by little modified the genius epidemicus.

The question arises whether the introduction of these new therapeutic principles has exerted its influence only on the course of the disease itself as manifested by the changing death rate and the incidence of complications, or on the very incidence of pneumonia itself.

While death rates are easily obtainable, statistical figures as to the epidemiological fluctuation of pneumonia and its complications can be determined only by means of a more intricate scrutiny, pneumonia being a non-reportable disease.**

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**The fact that lobar pneumoina is nominally a reportable disease obviously does not contribute much information as to the actual morbidity rate.

In a personal communication from the Board of Health of Wisconsin[1] we received the following mortality rates per 100,000 population by five year intervals:

	Under 1 year	1-4 years	5-9 years
1929-34	630.2	47.0	9.6
1934-39	456.9	33.3	5.5
1939-44	341.9	29.0	3.9
1944-49	203.6	9.8	1.5

The changes in the annual death rate from pneumonia per 100,000 total population since the influenza pandemic of 1918 have been summarized in the Statistical Bulletin of the Metropolitan Life Insurance Company of 1948.[2] It dropped from 575 per 100,000 in 1918 to 80 per 100,000 in 1930, to 70 (1936-37), to 46 in 1938 and to 17.4 in 1947.

According to the U. S. Summary of Vital Statistics of 1948[3] pneumonia and influenza changed places as the leading causes of death in the United States as follows: in 1920 the first leading cause of death, in 1930 second in the causes of death, in 1940 fifth, in 1948 the sixth leading cause of death.

A report from a General Hospital[4] covering all age groups gives the following drop in lobar pneumonia mortality: 1936-37, 23.3 per cent; 1940-41, 5.4 per cent; 1945-46, 6.5 per cent.

Another General Hospital[5] reports a decrease of deaths from pneumonia from 1937 on but the figures are too small to be significant.

A voluminous study of incidence and mortality rates in Helsinki, Finland,[6] covering the years from 1910 to 1945 presents a rather confused picture of "dropping off tendency of mortality" with an increased incidence of broncho-pneumonia between 1934 and 1942 which is ascribed to a possible change in "genius epidemicus."

In order to analyze, therefore, these changes in the occurrence and clinical course of various types of pneumonia, we have undertaken to go over a total of 5,927 cases of pneumonia which have been observed between the years 1929 and 1949 among 74,489 admissions to Milwaukee Children's Hospital.

The inpatient material of this hospital of between 135 and 150 bed capacity can be considered a fair cross section of the acute diseases in children of the Milwaukee area requiring hospitalization in any given year. The incidence of pneumonia per 100 hospital admissions throughout these 20 years should, therefore, offer a good indication of the epidemiological trends in childhood pneumonia.

Incidence of Pneumonia

First we determined the incidence of all types of pneumonia per 100 hospital admissions (See Figure 1).

It is surprising to find that there was a complete absence of a manifest trend toward a lower incidence of pneumonia, but merely a fluctuation over the 20 year period. The variations were between 5.2 to 11 cases per 100 admissions, but the averages of the four 5 year periods give the following figures: 8.0, 7 1, 7.7 and 8.7 per cent. This suggests to us that the introduction of the new antibacterial drugs, i.e., the sulfonamides and the antibiotics, were not instrumental in reducing the incidence of pneumonia in general.

In order to obtain more detailed information with regard to morbidity, the total figures were broken down into the following three groups: (1) lobar pneumonia, (2) broncho-pneumonia as the diagnosis on admission, (3) secondary broncho-pneumonia developing as a complication during the course of hospitalization.

It is quite obvious that the terms "lobar" as well as "bronchopneumonia" cover a large number of different pathological entities including atypical and virus pneumonia but excluding tuberculous pneumonia, sarcoidosis, fungal pneumonitis, pulmonary abscess and bronchiectasis. The two latter conditions will be considered in a subsequent chapter.

The apparent unyielding stability in the morbidity curve of all types of pneumonia lumped together following the introduction of the newer drugs may be attributed, at least partly, to viral infections. On the other hand, it seems surprising that the clinical impression on individual cases of being able to forestall the blossoming out of a systemic infection (respiratory, intestinal, urinary, etc.) into pneumonia by antibacterial therapy should not be borne out by observations on a large scale.

In breaking down the total figures three ways as outlined above we gain further insight into morbidity statistics.

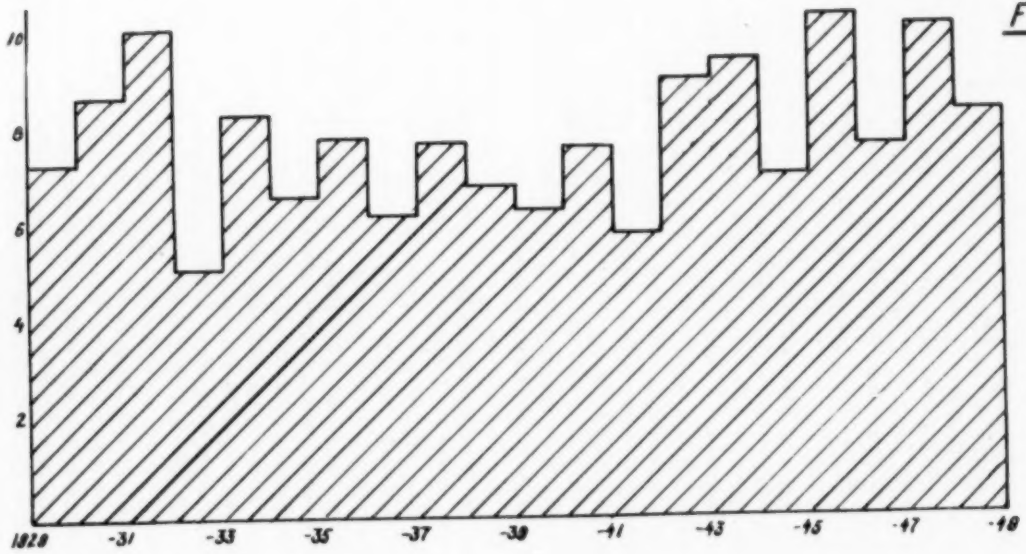
The incidence of lobar pneumonia per 100 admissions shows a fairly steady level from 1929 till about 1939. After this a definite decrease becomes manifest which for the last five year period appears as only a fraction of the previous rate (see Figure 2). The four quinquennial figures are as follows: 3.0, 3.5, 2.5, 1.2 per cent.

In contrast to this, the morbidity rates of all cases of broncho-pneumonia combined show a rather striking increase in frequency which is most marked for the last five year period from 1944 to 1949 (see Figure 3). Quinquennial figures: 5.4, 3.6, 5.3, 7.5 per cent.

In order to analyze this unexpected result, we computed the morbidity rates for primary and complicating broncho-pneumonia

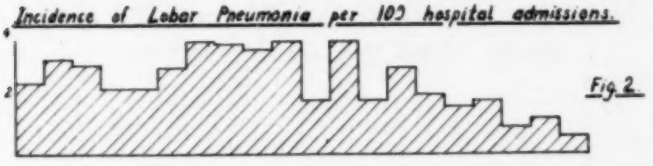
Incidence of Pneumonia (total) per 100 hospital admissions.

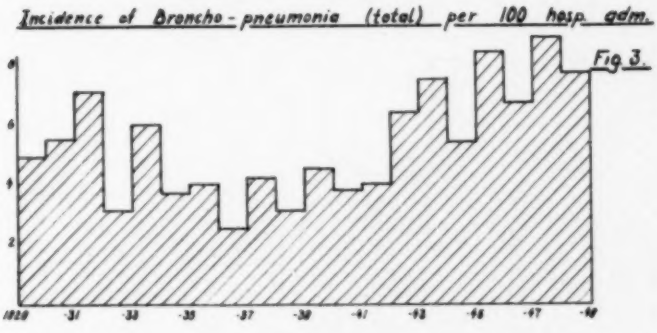
Fig. 1.

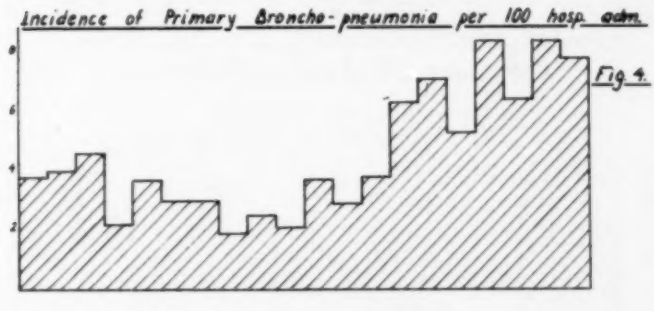


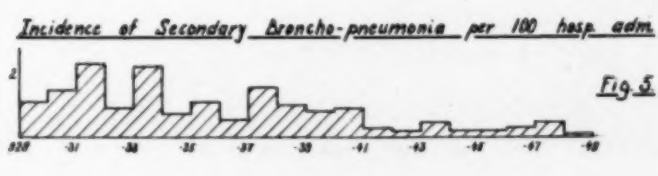
separately (see Figure 4 for primary broncho-pneumonia). Quinquennial figures: 3.7, 2.5, 4.8, 7.3 per cent.

This shows an even greater upward trend for primary broncho-pneumonia than that seen in Figure 3 for all broncho-pneumonia; the last five year period, which coincides with the most widespread use of antibiotics, shows an average incidence of 7.3 per cent as









compared, for instance, with 2.5 per cent in the five year period from 1934 to 1939, which were the years just before the ready availability of the sulfonamides.

On the other hand, the figures for broncho-pneumonia which developed as a complication during the hospital stay of children, comprising the entire range of childhood diseases including operative cases, show a decided decline coinciding roughly with the

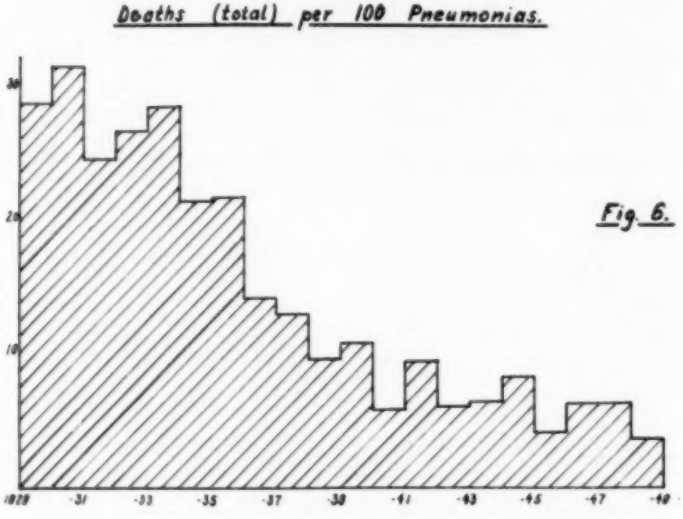


Fig. 6.

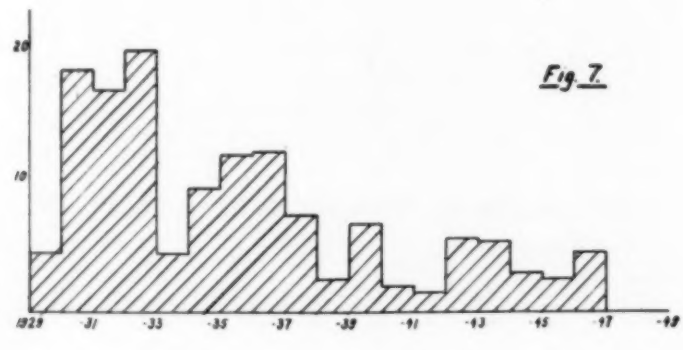


Fig. 7.

time of introduction of the sulfonamides and decreasing almost to the vanishing point for the last five year period (see Figure 5). Quinquennial figures: 1.7, 1.1, 0.6, 0.26 per cent.

These contrasting figures indicate that (1) hospital inpatients receive antibacterial agents prophylactically or early enough to

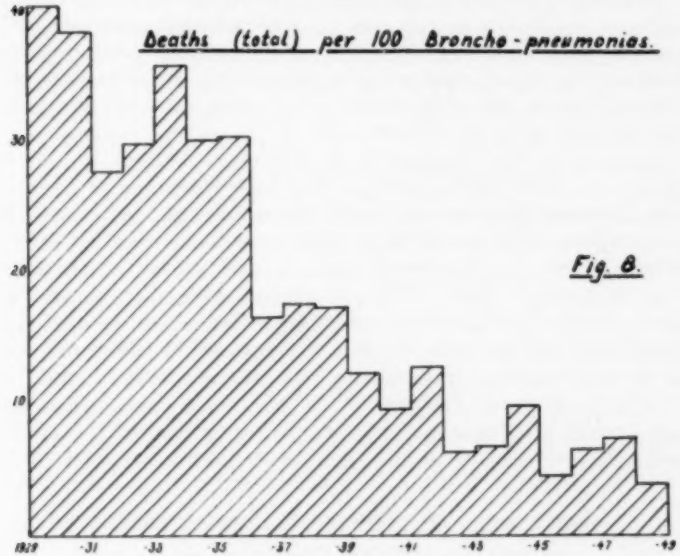


Fig. 8.

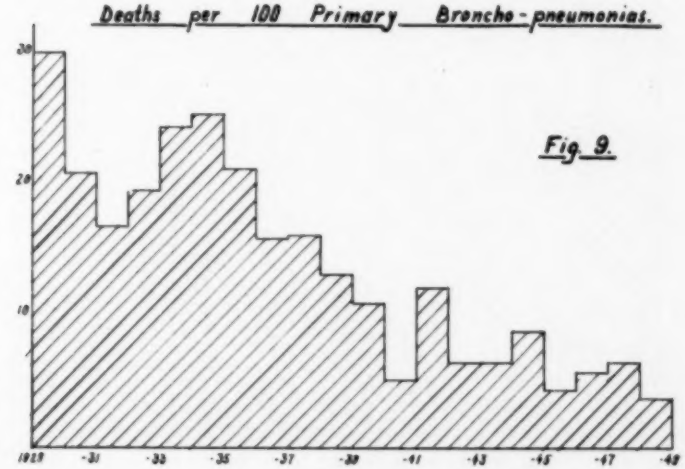


Fig. 9.

prevent extrapulmonary infections or other debilitating conditions from developing pneumonia, whereas (2) outpatients are either seen too late or treated inadequately.

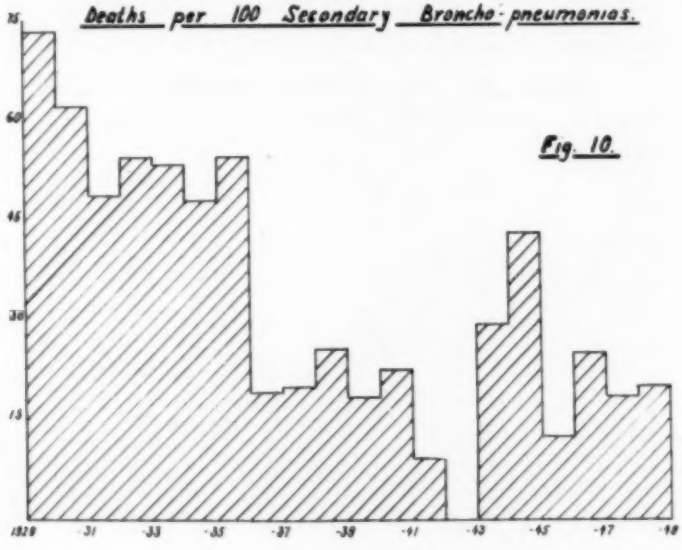
Effect on the Death Rate

The efficacy of the sulfonamides and antibiotics in the various types of pneumonia is well borne out in the declining death rate and our figures are very much in line with previous surveys. Figure 6 shows the first decided break in 1937 which coincides with the introduction of the sulfonamides on a larger scale. Quinquennial figures: 27.8, 16.0, 7.8, 5.9 per cent.

However, in lobar pneumonia alone (Figure 7), there is a sharp decline in 1933 which may have been due to the use of immune sera and immuno-transfusions. The decrease continued at a fairly steady pace, until the last two years had not one single death of lobar pneumonia. Quinquennial figures: 12.9, 8.8, 4.3, 2.0 per cent.

As to the death rate in primary broncho-pneumonia (Figure 9) the curve follows closely the total figures (Figure 8), because this form of the disease makes up, as a rule, between 50 and 80 per cent of all cases. Quinquennial figures: 34.6, 22.5, 9.6, 6.5 per cent.

Pneumonia as a complication of any underlying debilitating disease, including postoperative conditions, used to be one of the major contributors to infant mortality and the death rate of



secondary broncho-pneumonia at the beginning of our survey, i.e., from 1929 to 1936, was considerably greater than for primary pneumonia, either lobar or bronchial. However, during the ensuing years there was a decided drop in the death rate of secondary pneumonia which for the last few years appeared to be between one-third and one-fourth of the original figures. Quinquennial figures: 58.5, 33.3, 15.9, 24.0 per cent.

Along with the previously reported fact that the occurrence of these secondary pneumonias has been sharply curtailed, the lowered death rate constitutes a major achievement in preventive and curative medicine.

Incidence and Mortality of Empyema

As to the incidence of empyema following any type of pneumonia (Figure 11), we found the percentage fluctuating widely between 9.1 and 24 per cent. After 1938 the incidence declined definitely, and after 1940 sharply, until during the last five year period the rate was between one-tenth and one-twentieth of the earlier incidence. Quinquennial figures: 13.5, 14.7, 2.4, 1.0 per cent.

The mortality figures for empyema in five year periods are 17.9, 12.2, 31.8, 2.2 per cent. The unexpected rise during the period from 1940 to 1944 coincides with a sharp drop in incidence of empyema and seems to indicate that the most virulent micro-organisms causing pneumonia could not be controlled by sulfo-

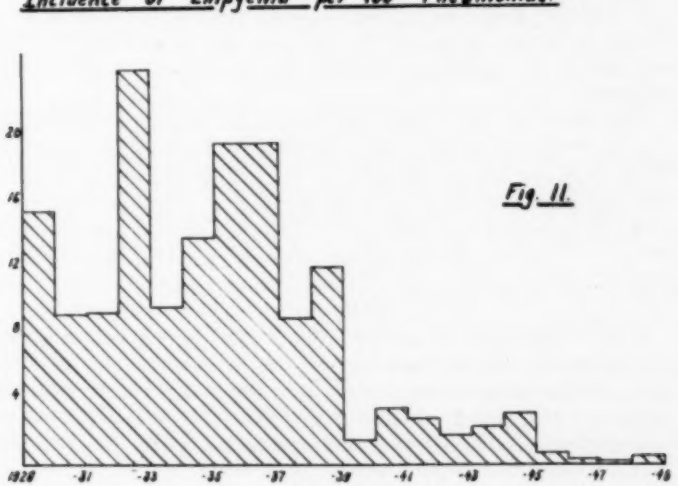


Fig. 11.

namide therapy to the point of preventing severe empyema with fatal outcome. However, the figures for the last five year period show that with increasing use of penicillin and allied antibiotics the mortality rate decreased to 2.2 per cent and for the last four years to 0 per cent.

Incidence of Bronchiectasis and Pulmonary Abscess

The paucity of clinically proved cases of bronchiectasis was surprising, the total over a period of 20 years being only 50 cases, which is less than seven in 10,000 admissions. Furthermore, the number has decreased steadily during the second half of our survey. Quinquennial figures: 18, 15, 8, 9.

There is, of course, always the possibility that some cases of bronchiectasis may have failed to be recognized on account of bronchography having been omitted. Yet the steady decline of bronchiectasis took place in spite of the increased availability of bronchography.

There were only six deaths among the 50 cases of bronchiectasis, and they were scattered over the 20 year period in a manner apparently unrelated to the introduction of the newer therapeutic measures.

Even more impressive is the scarcity of true pulmonary abscesses among the 74,489 admissions to our Children's Hospital; 43 cases were recorded. Counting them in four 5 year periods we see a sudden decline from 1936 on and an almost complete disappearance after 1944. Quinquennial figures: 27, 7, 6, 3.

The quinquennial death rate in this group of cases was 13 (i.e., 48.2 per cent) from 1929 to 1934; then it went down to 1, 4 and 3 deaths respectively which is not a favorable record considering the markedly lowered incidence rate of pulmonary abscesses.

It seems quite obvious that credit belongs to the widespread use of the several bacteriostatic biochemicals in reducing the morbidity in suppurative chest diseases like empyema, bronchiectasis and pulmonary abscess, a credit which also can be claimed for lobar pneumonia and secondary broncho-pneumonia, but definitely not for the large group which we termed "primary broncho-pneumonia."

Discussion

1) The impact of the introduction of antibacterial therapy on the incidence and mortality of respiratory infections and their more serious complications has been submitted to a thorough analysis by a review of 5,927 cases of pneumonia, 50 cases of bronchiectasis and 43 cases of pulmonary abscess out of 74,489 hospital admissions over a period of 20 years.

2) The introduction of the sulfonamides and antibiotic substances was apparently not instrumental in reducing the incidence of pneumonia in general. This may have been partly due to the inclusion of virus pneumonia.

3) The incidence of lobar pneumonia, however, shows a definite decline after 1939.

4) The total number of cases of broncho-pneumonia shows a striking increase per 100 hospital admissions, especially during the last five year period which coincides with the most widely accepted use of antibiotics, and this holds equally true for the type of cases we term primary broncho-pneumonia.

5) Secondary broncho-pneumonia which developed as a complication during the hospital stay of children with a wide range of diseases, both medical and surgical, shows a decided decline coinciding roughly with the time of introduction of the sulfonamides and decreasing almost to the vanishing point for the last five year period.

6) This discrepancy between the response to the newer therapeutic and prophylactic means, applied systematically and at the proper time, and the poorer results in the out-patient population at large seems to indicate that we are doing too little and too late in forestalling preventable broncho-pneumonia.

7) The progressive effect of the newer therapeutic measures on the death rate of all types of bacterial pneumonia, although not surprising or new, is most impressive. The least decline is shown by the fewer remaining cases of complicating or secondary pneumonia, but together with the previously reported sharp curtailment of these cases, the lower death rate adds up to a major achievement in preventive and curative medicine.

8) Postpneumonic empyema decreased from 13.5 per 100 cases from 1929 to 1934, to 1.0 per 100 from 1944 to 1949.

9) Cases of clinically proved bronchiectasis decreased from 25 for the first five years to seven for the last five years, seemingly a favorable response to the newer drugs. The very few deaths from bronchiectasis were scattered over the 20 year period, apparently unrelated to the newer therapeutic measures.

10) There were 43 cases of pulmonary abscess which is one out of 17,400 hospital admissions. There was a decided dropping off after 1936 and also a sharp decline in the death rate.

11) The actual lives saved from pneumonia death in half a generation is a tremendous number, but the hospital days saved through appropriate preventive procedures could have been more impressive if earlier and more adequate out-patient treatment had been given.

SUMMARY

A review of the incidence and mortality of 5,927 cases of pneumonia observed among 74,489 admissions to Milwaukee Children's Hospital over a period of 20 years has revealed the following trends:

1) The introduction of sulfonamides and antibiotic substances did not reduce the incidence of pneumonia in general. This may have been partly due to the inclusion of virus pneumonia.

2) The incidence of lobar pneumonia shows a definite decline after 1939.

3) Secondary broncho-pneumonia, as a complication during the hospital stay of children, also shows a marked decline and it decreased almost to the vanishing point during the last five years.

4) The death rate of all types of pneumonia has been sharply curtailed in recent years.

5) Postpneumonic empyema decreased from 13.5 per 100 cases of pneumonia from 1929-1934 to 1.0 per 100 from 1944-1949.

6) The occurrence of bronchiectasis and pulmonary abscess has become decidedly more rare and the mortality of the latter one has been sharply curtailed.

RESUMEN

La revisión de la incidencia y la mortalidad por neumonía entre 5,927 casos observados en 74,489 admisiones al Hospital de Niños de Milwaukee durante veinte años ha revelado las siguientes tendencias:

1) La introducción de sulfonamidas y de substancias antibióticas no redujo la incidencia de la neumonía en general. Esto en parte puede deberse a que se incluyó la neumonía de virus.

2) La incidencia de la neumonía lobar muestra una de clinación definida después de 1939.

3) La bronconeumonía secundaria como complicación de la estancia de los niños en el hospital muestra también una de clinación marcada y decreció casi hasta desaparecer durante los últimos cinco años.

4) La mortalidad en todos los tipos de neumonía se ha reducido decididamente en los últimos años.

5) El empiema post-neumónico decreció de 13.5 por ciento de los casos de neumonía de 1929 a 1934, a 1.0 por ciento de 1944 a 1949.

6) La bronquiectasis y el absceso pulmonar se han hecho francamente mas raros y la mortalidad del último se ha limitado decididamente.

RESUME

Un compte rendu sur l'incident et la mortalité de 5,927 cas de pneumonie observés parmis 74,489 d'admissions par l'Hôpital

d'Enfants de Milwaukee, Wisconsin au cours de vingt ans indique les conclusions suivantes:

1) L'introduction des sulfonamides et des substances antibiotiques n'a pas diminué l'incident de la pneumonie en general. Il ce peut que ce resultat a été reçue en y comprenant aussi les pneumonies virus.

2) Les cas de pneumonie lobaire ont définitivement diminués après 1939.

3) Le nombre des broncho-pneumonies secondaires, se presentant pendant le séjour d'un enfant malade a l'hôpital, a beaucoup decliné jusqu'au point de disparaitre presque complètement au cours des 5 ans passés.

4) Le nombre de pneumonies fatals à été reduit très évidémment pendant les années précédantes.

5) L'empyeme apres la pneumie a diminué en nombre de 13.5 dequis 1929-1934 jusqu'a 1 per 100 de 1944-1949.

6) L'incident de bronchiectasie et abscès pulmonaire est decidémment plus rare, et la mortalite du cas dernier a été reduit drastiquemment.

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Anomalies of the Pulmonary Veins: Their Surgical Significance

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The reports of anomalies of the pulmonary veins are appearing more frequently in the medical literature. The earliest recognition of the condition was a rarity found at the postmortem examination or in the anatomic laboratory. Later, intrathoracic operations led to its recognition during life.[1] The greatest and most important advance in the recognition of the condition was made by the use of angio cardiography and cardiac catheterization.

The various types of pulmonary vein anomalies can be divided into two great categories. In the first and less important group the pulmonary venous drainage is normal but there is an abnormal number of pulmonary veins draining the lungs: in the second and more important group the pulmonary venous drainage is abnormal into the right atrium or one of its tributaries, comprising either (a) a part of the pulmonary venous blood or (b) the total pulmonary venous blood from both lungs.

Where the anomaly is found merely in the number of veins that drain normally into the left auricle, the thoracic surgeon must be alert to the possibility of a single vein draining the whole lung on either the right or left side. When the condition is unrecognized the whole lung may be devitalized in doing a single lobectomy. A single pulmonary vein that drains the lung is seen more frequently on the left side. During surgery the author has found eight instances of a single pulmonary vein on the left side and six on the right side. If the pulmonary veins are studied inside the pericardium a single vein draining the whole lung will be found more frequently.

Abnormal drainage of pulmonary venous blood into the right atrium or its tributaries in part or in the whole is, of course, the most important aspect of anomalous pulmonary veins. Dotter, Hardisty and Steinburg reported a total of 133 cases appearing in the literature and added two more of their own. Not included in the total were two more cases, one each described by Young[4] and Johnson and McRae.[2] At intrathoracic operations the author has observed two additional patients with drainage of venous

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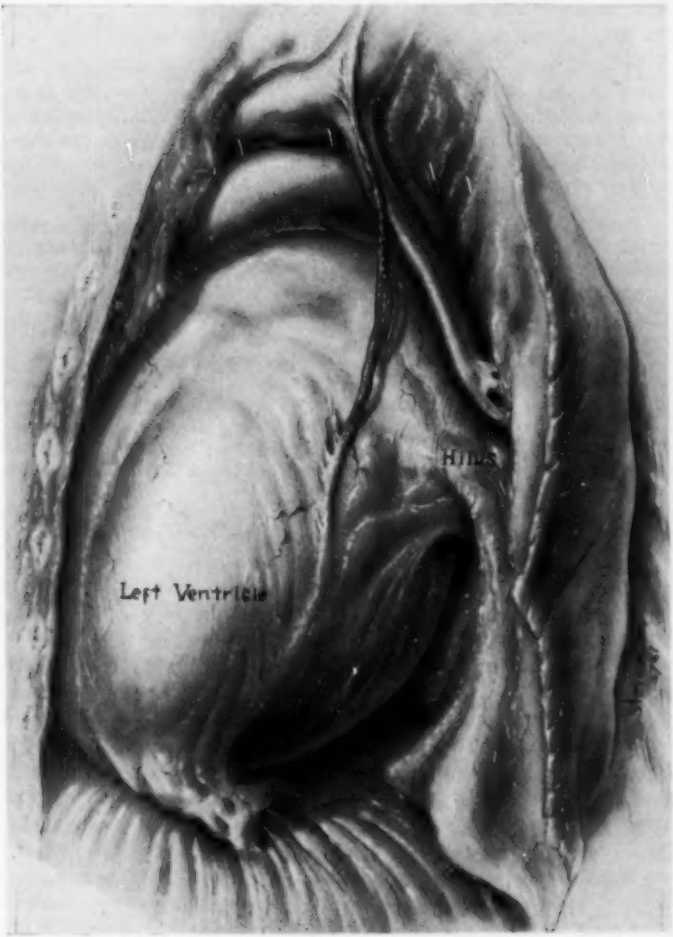

FIGURE 1: The drawing shows the left pleural cavity. The upper lobe of the left lung is drained by the junction of three segmental veins into a common trunk which in turn drains into the left innominate vein. The left phrenic nerve has the same relationship to this anomalous vein as the right phrenic nerve has to the superior vena cava.

blood from the upper lobe of the left lung into the left innominate vein. Since the findings in both instances were identical only one case is described.

Case Report

J.O.E., a white male, age 49 was admitted to University Hospital because of impending external perforation of a traumatic aneurysm of the left common carotid artery. This artery was ligated and divided where it branched from the aorta and at its bifurcation into the two terminal arteries. The patient made an uneventful recovery. The left side of the chest was opened with the patient in the lateral position and the superior mediastinum was similar to that on the right side (Figure 1). There appeared to be a superior vena cava with a phrenic nerve running parallel to it. The subclavian artery was deep to this venous structure and was not visible. Of course, as the hilum was approached there was no azygos vein and the aorta came into view. The anomalous venous structure that appeared to be a superior vena cava was lateral to the descending aortic arch and anterior to the root of the lung, and was easily dissected free. It originated from the junction of three segmental veins from the upper lobe of the left lung. The segmental veins joined to form the anomalous vein anterior to the root of the upper lobe. It emptied into what appeared to be a normal left innominate vein. There was a normal appearing inferior pulmonary vein draining the lower lobe. No other vein drained the upper lobe of the lung. This anomalous vein of the upper lobe of the left lung is shown in the drawing in Figure 1.

Dotter, Hardisty and Steinburg[3] were the first to diagnose the anomalous pulmonary venous drainage in the living without the aid of intrathoracic operation. The ability to diagnose the anomaly will in the future undoubtedly lead to therapy when needed. Where only one lobe drains into the systemic venous system it is difficult to believe any abnormal symptoms will appear. Sweet[5] and Stansbury[6] have partially created the condition in their surgical procedure in mitral stenosis by joining the superior segmental vein of the lower lobe of the right lung to the axygos vein. Where the whole lung drains into the right atrium or venous system it is readily conceivable that right heart strain or even right cardiac failure is likely to occur, particularly as the patient grows older. Where formerly the author and later Dotter, Hardisty and Steinburg suggested lobectomy or pneumonectomy to alleviate the condition, it is obvious that ligation of the pulmonary artery leading to the lung with the anomalous venous drainage would accomplish essentially the same purpose. It would be a lesser surgical procedure and there would be no change in space relationships within the thorax. For a patient showing signs of cardiac failure anastomosis of the pulmonary vein into the left auricle would probably be more surgery than the patient could tolerate. The ability to diagnose the drainage of pulmonary venous blood from one lung into the systemic venous system will prevent the thoracic surgeon

from removing the normal lung that is maintaining oxygenation for the patient.

Where there is drainage of the total pulmonary venous blood from both lungs into the right auricle or its tributaries it is incompatible with life unless there are associated cardiac anomalies. From reports in the literature it appears that death usually occurs when the foramen ovale closes. Patients presenting this anomaly have been stillborn or have died within a few months after birth, except in one case reported by Taussig.[7] This patient died at the age of four years and the autopsy showed total pulmonary venous drainage of both lungs into the vena cava. The foramen ovale was physiologically patent but the size of the opening was not given. There was no evidence of cyanosis during life. A patient able to live four years probably would survive if by the method described by Blalock[8] an adequate intra-atrial septal defect were produced. In the future some surgeon surely will diagnose the anomaly in a newborn infant and perform successful surgery. One can also speculate on other methods of changing the venous circulation to make it compatible with life.

SUMMARY

Anomalous pulmonary venous drainage can be diagnosed in the living patient by angiocardiography, cardiac catheterization, and by surgical exposure.

With the recognition of abnormal pulmonary venous drainage in the living it seems likely that symptoms developing from this condition will be relieved by surgical intervention.

RESUMEN

El tránsito venoso anómalo en las venas pulmonares puede ser diagnosticado en el vivo por la angiocardiografía, el cateterismo cardiaco y la exposición quirúrgica.

Con el conocimiento del tránsito venoso pulmonar anómalo en el vivo, es posible que los síntomas dependientes de estas anomalías puedan ser aliviados por una intervención quirúrgica.

RESUME

Les anomalies de la veine pulmonaire peuvent être diagnostiquées sur le vivant par angiocardiographie, cathétérisme cardiaque, ou par thoracotomie exploratrice.

Lorsqu'on a mis en évidence une anomalie du courant de la veine pulmonaire, il semble que les symptômes consécutifs à ces troubles puissent être supprimés grâce à la chirurgie.

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Incidence of Tuberculin Reactors in a Series of 2,000 Patients Seen in a Private Practice of Internal Medicine

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This is a study of the incidence of reactors to tuberculin in a series of 2,000 consecutive patients seen in our private practice of internal medicine.

The tuberculin test as an aid in the diagnosis of tuberculosis, has become more useful since the percentage of reactors has steadily decreased each year. In years past it was thought that the test was of little value in adults because practically all reacted. The reason[1] being that in the early part of the century most adults had been infected with tubercle bacilli. As the drive[2] to stamp out tuberculosis became more effective, the number of tuberculin reactors decreased so that now there are many adults who do not react. This enhances the usefulness of the test as a diagnostic procedure.

The technique used was the intradermal injection of 0.1 cc. of a 1:1000 solution of old tuberculin provided by the Minnesota Department of Health. The intradermal injection produced a bleb which would sting immediately after administration. The test was read in 72 hours. A reaction[3] is an area of edema or induration not less than 5 mm. in diameter. This was read by palpation. Suspected cases of tuberculosis who did not react to the first dose were given a second injection of 0.1 cc. of 1:100 solution of old tuberculin.

The best criteria of the effectiveness of tuberculosis control leading to the eventual eradication of the disease is found in the incidence of tuberculin reactors. In the[4] United States, it is now estimated that definitely less than 50 per cent of the population would react to tuberculin if tested. In Detroit, for instance, Douglas and Harmon, in 1938, reported tuberculin testing of 99,414 people among whom the percentage of reactors varied from 6.9 per cent below the age 10 to 44.3 per cent among those of 30 years or older. Testing of grade school children in Minneapolis, in 1926, revealed 47.3 per cent reactors. In 1936, this was 18.9 per cent and in 1944, only 7.7 per cent. In 1944, only 2 per cent of children of 6 years of age reacted. Testing students upon admission to the University of Minnesota was first begun in 1928. That year approximately

33 per cent reacted to tuberculin. This was reduced to 19.3 per cent for the school year 1946-1947, to 15.7 per cent for 1947-1948, and to 11.2 per cent for 1948-1949. The Minnesota[5] Department of Health, during the year 1949, tuberculin tested 38,777 school children from kindergarten through the 12th grade and found only 1,262 reacted (3.25 per cent). In 1946-1947, Jordon[6] found that among 3,698 adults in the Riverside Sanatorium District, in Minnesota, ranging from 21 to 74 years of age, only 21.6 per cent reacted to tuberculin. During the same period of time he found only 2.7 per cent reactors among 12,666 children tested with tuberculin as compared with an average of 13.9 per cent of the children tested from years 1930-1934 in the same district. He has reduced the incidence of tuberculin reactors among children so much that in the entire 277 schools of his four counties' sanatorium district, in 1946 and 1947, there were no reactors in 219 of these schools. Danielson's[7] report on the Meeker County Tuberculosis Control Project, in Minnesota, undertaken during the years 1941-1942, showed among the 10,733 persons tested 2,445 (22.8 per cent) reacted to tuberculin.

Of our 2,000 patients tested, 779 were males and 1,221 were females. They were largely city dwellers in Minnesota. The overall incidence of tuberculin reactors in this group was 55.6 per cent. The incidence by decades is shown on Chart I. The incidence for the 0-9 decade was 11 per cent and for the 10-19 decade 15 per cent. Thus in the childhood and adolescent periods in life only 13.8 per cent reacted to tuberculin. The number of children in this series was small. The incidence of tuberculin reactors

CHART I: ALL PATIENTS

Decades	MARITAL STATES				REACTORS		Non Reactors		Total Patients
	Married	Single	Widowed	Divorced	Number	Pct.	Number	Pct.	
0-9	..	47	..	..	5	11	42	89	47
10-19	13	127	..	..	21	15	119	85	140
20-29	208	182	2	13	154	38	251	62	405
30-39	304	68	6	11	210	54	179	46	389
40-49	298	45	20	17	256	66	124	33.5	380
50-59	267	30	41	8	263	76	83	24	345
60-69	127	22	50	12	149	71	62	29	211
70-79	33	3	32	..	47	69	21	31	68
80-89	3	2	8	1	8	57	6	43	14
Total	1253	526	159	62	1113	55.6	887	44.4	2000
Per cent	62.7	26.3	7.95	3.1					

increased from 38 per cent in the 20-29 decade as shown on Chart I to 76 per cent in the 50-59 decade. This gradually declined to 57 per cent among those from years, 80-89. The number of patients in the latter decade was also small. Among those from 20-89 years, the incidence of reactors was 59.9 per cent. Of these 2,000 patients 62.7 per cent were married, 26.3 per cent were single, 7.95 per cent were widowed, and 3.1 per cent were divorced. There is apparently no relation between the marital state of the patient and the tuberculin reaction.

CHART II: ALL FEMALES

Decades	MARITAL STATES				REACTORS		Non Reactors		Total
	Married	Single	Widowed	Divorced	Number	Pct.	Number	Pct.	Females
0-9	..	24	..	..	2	8.3	22	92	24
10-19	12	84	..	..	14	14.6	82	85.4	96
20-29	136	118	1	7	94	36	168	64	262
30-39	186	44	6	5	125	52	116	48	241
40-49	159	28	16	12	141	66	74	34	215
50-59	148	16	35	7	161	73	45	27	206
60-69	61	12	43	8	82	67	42	33	124
70-79	13	2	30	..	31	73	14	27	45
80-89	..	1	6	..	4	50	4	50	8
Total	715	329	137	40	654	53.5	567	46.4	1221
Per cent	66.7	26.9	11.2	3.2					

CHART III: ALL MALES

Decades	MARITAL STATES				REACTORS		Non Reactors		Total
	Married	Single	Widowed	Divorced	Number	Pct.	Number	Pct.	Males
0-9	..	23	..	..	3	13	20	87	23
10-19	1	43	..	..	7	16	37	84	44
20-29	72	64	1	6	60	42	83	58	143
30-39	118	24	..	6	85	57	63	43	147
40-49	139	17	4	5	115	64	50	36	165
50-59	119	14	6	1	102	73	38	27	140
60-69	66	10	7	4	67	77	20	23	87
70-79	20	1	2	..	16	69	7	31	23
80-89	3	1	2	..	4	67	2	33	6
Total	539	197	22	22	459	58.9	320	41.1	779
Per cent	69.0	25.2	2.8	2.8					

The female patients numbered 1,221; and the results of tuberculin testing by decades are shown on Chart II. The incidence is essentially the same for both males and females. In the 0-9 decade 8.3 per cent reacted and in the 10-19 decade 14.6 per cent. The incidence for the first 19 years of life among the females was 13.3 per cent. The incidence gradually rose from 36 per cent in the 20-29 decade to 73 per cent in the 50-59 decade and in the 70-79 decade. It fell to 50 per cent in the 80-89 decade. The incidence of reactors from the ages 20 to 89 was 57.9 per cent.

The male patients numbered 779, and showed an overall incidence of 58.9 per cent reactors to tuberculin. This is shown on Chart III. The 0-9 decade showed an incidence of 13 per cent and the 10-19 decade 16 per cent reactors. Thus the incidence of reactors among the male patients in the first 19 years of life was 14.9 per cent. There was a rise from 42 per cent in the 20-29 decade to 77 per cent in the 60-69 decade, and a decline to 67 per cent in the 80-89 decade. The number of patients in the 0-9 and 80-89 decades were small. The incidence of reactors from ages 20 to 89 was 63.1 per cent.

SUMMARY

1) The over-all incidence of reactors to tuberculin was 55.6 per cent among 2,000 consecutive patients seen in our practice of internal medicine.

2) The incidence among the 1,221 females was 53.5 per cent and among the 779 males it was 58.9 per cent.

3) The average incidence of tuberculin reactors among persons from 20 to 89 years was 59.9 per cent, and those from 0 to 19 years was 13.8 per cent. The younger the individual the less likely is he to be a reactor to tuberculin.

4) The tuberculin test is an important, single diagnostic procedure to discover those infected with tubercle bacilli.

5) The high number of tuberculin reactors in this group is because of the fact that many of these patients were being studied because of lung disease, and yet here the tuberculin test proved to be a most valuable rapid screening method to exclude the presence of tuberculosis.

RESUMEN

1) La incidencia total de reactores a la tuberculina fué de 55.6 por ciento entre 2,000 enfermos consecutivos vistos en nuestra práctica de medicina interna.

2) La incidencia entre 1,221 mujeres fué de 53.5 por ciento y entre 779 hombres de 58.9 por ciento.

3) La media de reactores a la tuberculina en personas de 20 a

89 años fué de 59.9 por ciento y la de aquellos entre 0 y 19 años fué de 13.8 por ciento.

4) La reacción tuberculínica es un procedimiento sencillo e importante para descubrir a los infectados con bacilo de la tuberculosis.

5) El alto número de reactores a la tuberculina en este grupo se explica porque muchos de estos enfermos fueron estudiados en vista de que tenían alguna enfermedad del pulmón y así se mostró la reacción tuberculínica como medio valioso y rápido para excluir la tuberculosis.

RESUME

1) La fréquence générale des réactions positives à la tuberculine fut de 55.6% parmi les 2,000 sujets examinés.

2) La fréquence fut de 53.6% pour 1,221 femmes, et de 58.9% pour 779 hommes.

3) La fréquence moyenne des tests positifs pour les sujets de 20 à 89 ans est de 59.9% et pour ceux de 0 à 19 ans de 13.8%. Plus l'individu est jeune, moins il est sujet à avoir une réaction tuberculinique positive.

4) Le test tuberculinique est un élément capital de la découverte de l'infection tuberculeuse.

5) Le nombre élevé de réactions positives dans le groupe étudié est dû au fait que beaucoup de ces malades étaient atteints en réalité d'affection pulmonaire. Dans ces cas, la réaction à la tuberculine s'est avérée être une méthode précieuse et rapide pour exclure le diagnostic de tuberculose.

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Coexistent Bronchogenic Carcinoma and Active Pulmonary Tuberculosis*

A Report of Five Cases with Autopsy Findings

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There is a divergence of opinion as to the frequency of active pulmonary tuberculosis and primary carcinoma of the lung. Until recently the occurrence of the two diseases in the same patient was considered rare. Earlier observers were of the opinion that carcinoma and tuberculosis were incompatible, and that an element of antagonism existed between them.[1,2] Others have pointed out that tuberculosis, like any other chronic inflammation or irritation, predisposed to the development of carcinoma as a result of cellular metaplasia of the bronchial and alveolar epithelium.[3,4]

In the past four years, in the Veterans Administration tuberculosis hospital at Castle Point, New York, there have been five instances among 203 autopsies in which active pulmonary tuberculosis was found in association with bronchogenic carcinoma. The patients were white males, World War I veterans ranging in age from 48 to 61 years. In three, the carcinoma was diagnosed during life; in the other two it was discovered at autopsy.

The following are the summaries of the five case histories, with the pertinent autopsy findings:

Case 1: F.W., 52 years old, was admitted to the hospital because of "burning sensation" in the right side of the chest and recurrent hemoptyses. Tuberculosis had been diagnosed 19 years previously. Since then he had frequent episodes of blood streaked sputum followed by brief periods of hospitalization at various institutions. Chest x-ray films taken one year prior to present entry, showed evidence of cavitation in the right upper lobe with slight dissemination to the right lower (Figure 1a). The chest x-ray film at the time of the final admission to the Veterans Administration hospital, Castle Point, revealed a marked increase in size of the cavity in the right upper lobe with a fluid level. New infiltrations were present below this area (Figure 1b). The sputum contained acid fast bacilli on repeated examinations. His temperature fluctuated between 99 and 101 degrees F. An x-ray film taken two months later

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showed extension of the disease to the right lower lobe. The condition became progressively worse and five months after admission he had a massive hemoptysis and died.

At autopsy the right main bronchus was markedly narrowed by a firm gray-yellow mass which extended into the cavity in the right upper lobe and into the surrounding peribronchial lymph nodes. On histologic examination the bronchial wall was almost completely replaced by many irregular sheets of epithelial cells with some pearl formation. In one area, the tumor cells (squamous cell carcinoma) extended directly into the right upper lobe.

The right upper lobe contained several large interlocking cavities with bronchi opening into these cavities. The horizontal branch of the left upper lobe bronchus was completely stenosed by firm bands of tuberculous scar tissue. Caseous and fibro-caseous foci were present throughout the entire left lung and right upper lobe. Miliary tubercles were found in the kidney, spleen, liver and adrenals.

Case 2: J.W., 48 years old, was admitted because of cough, weakness, right side of chest pain, fever and weight loss. Three months prior to entry, he had "grabbing" pain on the right side not affected by respiration. He appeared emaciated and ill. The sputum contained numerous acid fast bacilli. The chest x-ray film (Figure 2) revealed evidence of extensive caseous pneumonic consolidation of the right upper lobe with multiple cavities. During hospitalization his fever ranged from 99 to 102.8 degrees F. He complained of severe cough and dyspnea. On the 15th hospital day, streaked sputum was noted for the first time. The following day he had a massive pulmonary hemorrhage and died.

At autopsy there was a tumor mass (5 cms. in diameter) on the right lateral aspect of the trachea (4 cms. above the carina) which narrowed the lumen. It involved both trachea and right main bronchus. Some of the tumor tissue had extended into and eroded the roof of the tuberculous cavity wall in the right upper lobe. A branch of the pulmonary

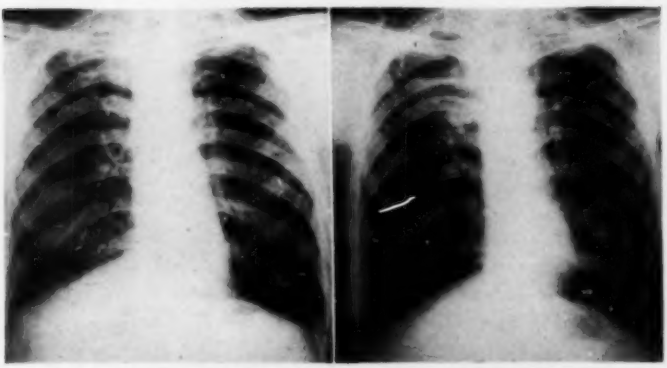


FIGURE 1a FIGURE 1b

Figure 1a, Case 1: November 20, 1945. Bilateral pulmonary tuberculosis, cavity in right upper lobe.—*Figure 1b, Case 1:* May 18, 1946. Large cavity with fluid level; bronchial neoplasm discovered at autopsy.

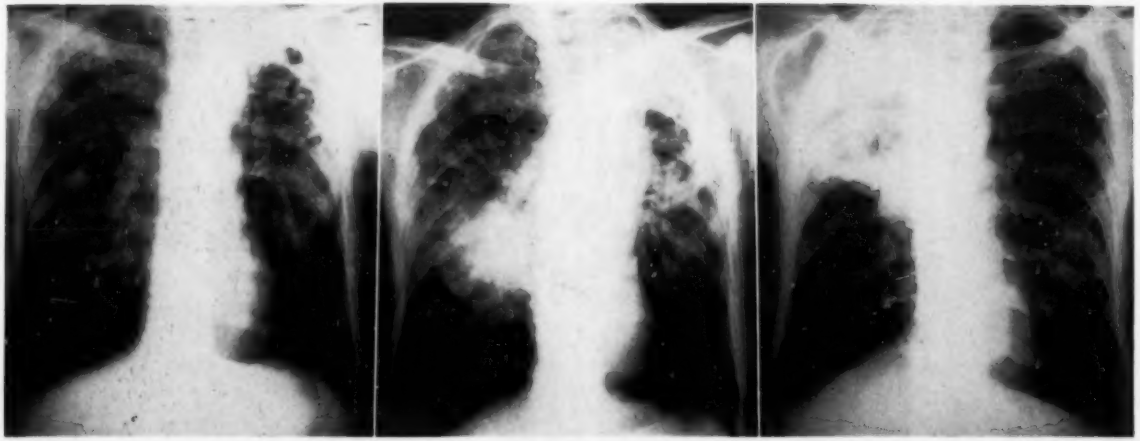


FIGURE 3a FIGURE 3b FIGURE 2

Figure 2, Case 2: Caseous pneumonic consolidation of right upper lobe with multiple cavities, spread to left lower lobe. Illustrates difficulty in diagnosis of associated carcinoma from a single film. — *Figure 3a, Case 3:* March 6, 1942. Bilateral pulmonary tuberculosis, cavity left upper lobe, spread to lower lobe.—*Figure 3b, Case 3:* April 15, 1949. Circular density in right mid-lung field, atypical for caseous pneumonia or tuberculous spread, diagnosed carcinoma, right lower lobe.

artery to the right upper lobe had become eroded by the carcinoma causing the fatal hemorrhage.

On histologic examination of the tissues the tracheal wall was found completely replaced by typical squamous cells which extended irregularly into the lumen. Gelatinous pneumonia (tuberculous) was found in the lower lobe of the left lung.

Case 3: J.A.M., 61 years old, was admitted to the hospital because of weakness, poor appetite and shortness of breath. Tuberculosis was first diagnosed seven years previously. Two years after the onset of illness he entered the Veterans Administration hospital at Castle Point because of disease in the upper lobes. The sputum contained acid fast organisms. After several weeks he left the hospital against medical advice. During the next four years there followed alternate periods of work and hospitalization at various institutions (Figure 3a). At the time of the second admission he complained of severe shortness of breath, intermittent localized sharp pain behind the sternum, cough and expectoration of a quarter of a cup of sputum daily. The chest x-ray film at the time of the final admission (Figure 3b) showed evidence of multiple cavities in the upper two thirds of the left lung and scattered foci in the right upper lobe. In the right mid-lung field, there was seen for the first time a circumscribed circular density. Tumor was suspected and inasmuch as he was too ill for bronchoscopy, the sputum was examined repeatedly for malignant cells (Papanicolau stain) but none were found. His condition became progressively worse and he died three months after admission and seven years after the onset of pulmonary tuberculosis.

Autopsy revealed a large fairly circumscribed tumor mass in the right lower lobe just below the interlobar fissure in the postero-lateral aspect. It was solid white and pink in color. The cut surface presented areas of softening and hemorrhage. In the anterior aspect of this lobe and independent of the tumor mass, there were present many caseous and fibrocaseous foci. In the right upper and middle lobe, were also scattered caseous foci. The left upper lobe, and to a lesser extent the left lower

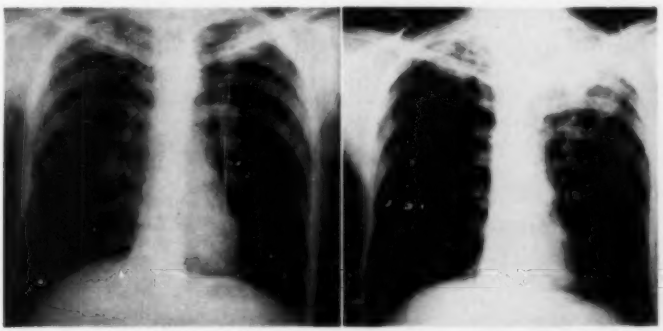


FIGURE 4a FIGURE 4b

Figure 4a, Case 4: September 29, 1942. Bilateral upper lobe pulmonary tuberculosis.—*Figure 4b, Case 4:* June 6, 1949. Dense solid lesion upper third left lung atypical for progressive pulmonary tuberculosis; diagnosis pulmonary neoplasm.

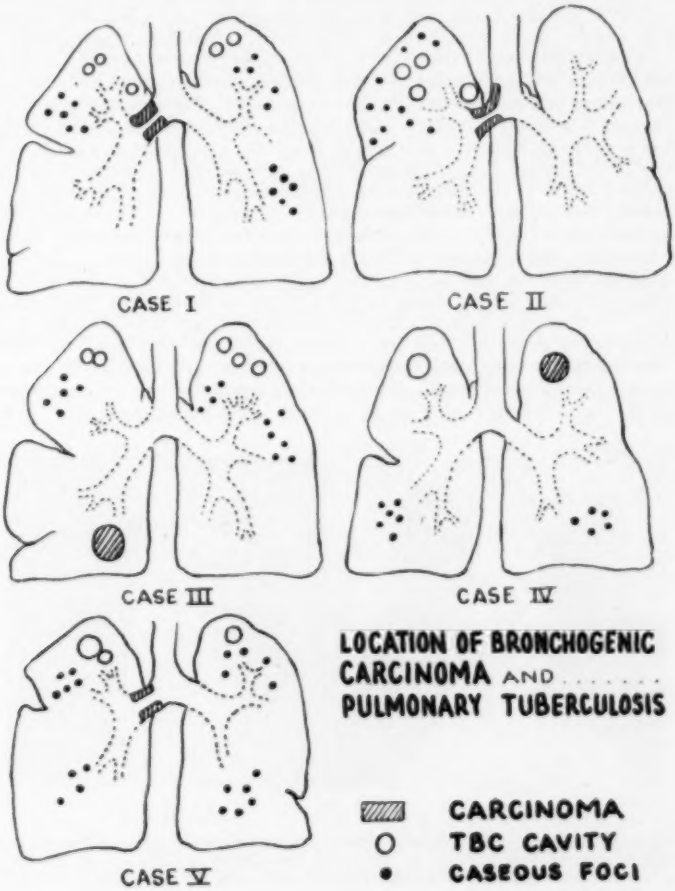
TABLE I

SUMMARY OF PERTINENT AUTOPSY FINDINGS

		DURATION		LOCATION				
Name	Age	Tuberculosis	Carcinoma	Tuberc.—Type	Carcinoma	Type Carcinoma	Metastasis	Cause of Death
Case 1 (FW)	52	19 years	?	Cavity RUL, LUL. Caseous and Acino-Nodose Foci. RUL, LUL, LLL. Acute Miliary: RLL, LLL, liver spleen, kidney, adrenal	Right Main Bronchus	Squamous	Cavity RUL, Rt. Pleura, Rt. Peri-bronchial nodes	Carcinoma Massive hemoptysis
Case 2 (JW)	48	4 months?	4 months?	Cavities RUL. Tbc. Pneumonia LLL	Trachea and Right Stem Main Bronchus	Squamous	Rt. Superior Tracheo-Bronchial Lymph Nodes Rt. Upper Lobe Adrenals	Carcinoma Massive hemoptysis
Case 3 (JAM)	61	7 years	3 years?	Cavity RUL, LUL, LLL. Caseous Foci all lobes	Right lower lobe	Undifferented (anaplastic)	Rt. Inferior Tracheo-Bronchial Lymph Nodes	Carcinoma and Pul. Tbc.
Case 4 (JT)	54	10 years	1 year?	Cavity RUL, RLL, Caseous Foci Rt. lung LLL	LUL	Adeno-Carcinoma	Pleura, Left Peri-Bronchial Lymph Node. Erosion left 3rd rib	Carcinoma (Cachexia)
Case 5 (HPB)	50	17 months?	17 months?	Cavity, RUL, LUL, RLL. Caseous Foci all lobes	Right Main Bronchus	Squamous	Regional Lymph Nodes Right lower lobe	Carcinoma Massive hemoptysis

lobe, contained multiple tuberculous cavities and scattered caseous foci. On histological examination the tumor revealed considerable anaplasia of the cells, the latter being arranged in masses and sheets surrounded by thin fibrous stroma.

Case 4: J.T., 54 years old, became ill three years prior to admission to the hospital. The initial x-ray film revealed evidence of bilateral upper lobe cavitation. The sputum was persistently positive for acid fast bacilli. No definitive treatment was administered. The disease remained stationary (Figure 4a) for six years. Then he began to complain of persistent dull aching pain in the left upper chest. On x-ray film inspection (Figure 4b) evidence of a dense solid lesion was seen in the upper third of the left lung. A Bucky film revealed erosion and thinning of the 3rd left



posterior rib. Because tumor was suspected, material was obtained by needle biopsy as well as from bronchoscopic aspiration. No tumor cells were found by the Papanicolau method. He died eight months later.

At autopsy a firm hard yellowish white tumor mass 9 x 7 cm. was present in the postero-apical aspect of the left upper lobe. Strands of white tumor tissue extended into the lung parenchyma of this lobe and several small abscesses were found in this area. There were several interlocking cavities in the right upper lobe and a cavity was present in the apex of the left lower lobe. Small caseous and fibro-caseous foci were diffusely scattered throughout the entire right lung as well as in the left lower lobe.

On histological preparation, the tumor in the left upper lobe was found to be a well differentiated adenocarcinoma.

Case 5: H.P.B., 50 years old, was admitted because of increasing fatigue and general ill-health of about three months duration. The admission x-ray film showed a lesion in the right upper lobe. The sputum contained acid fast bacilli. A chest x-ray film three months later revealed evidence of two cavities in the right upper lobe (Figure 5a). He left the hospital but was readmitted eight months later because of chest pain, hoarseness, asthmatic seizures, intermittent hemorrhages and weight loss of 15 pounds. X-ray film inspection then showed an increase in size of the cavities in right upper lobe, a small cavity in left apex and a new density in the upper right mediastinum (Figure 5b). One month after readmission, and 17 months after the clinical onset of his tuberculosis, the patient had a massive pulmonary hemorrhage and died.

At autopsy, the wall of the right main bronchus was thickened and infiltrated with tumor tissue, causing partial stenosis. The right lower lobe, in its postero-lateral aspect had many sharply circumscribed yellowish white tumor nodules and a small cavity was present at the base.

In the right upper lobe, there was a large cavity (7 cms. in diameter) in its postero-lateral aspect. Anteriorly, there were many smaller cavities which communicated with an open bronchus. The left lung had many

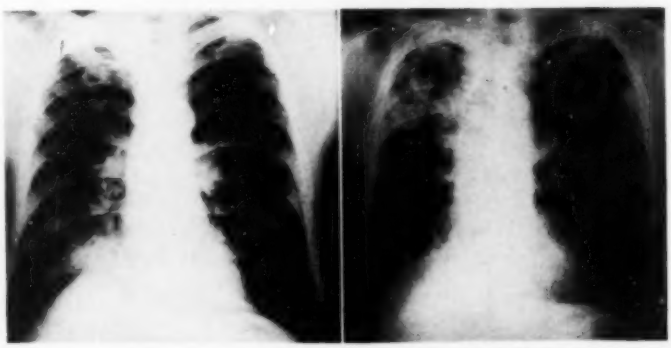


FIGURE 5a FIGURE 5b

Figure 5a, Case 5: June 26, 1947. Pulmonary tuberculosis, two cavities, right upper lobe.—*Figure 5b, Case 5:* March 28, 1948. Giant cavity and new shadow right upper mediastinum suggestive of associated neoplasm.

scattered caseous foci in both lobes, a small cavity but no evidence of malignancy.

Histological examination of the right main bronchus revealed marked infiltration with tumor cells of the squamous type.

Discussion

There are many difficulties associated with the diagnosis of primary lung cancer in patients with active pulmonary tuberculosis. The tuberculous process usually dominates the clinical picture for a number of years so that the development of malignant growth is easily overlooked. Furthermore, the two diseases may closely resemble each other.[5] A localized unilateral wheeze may be attributed to tuberculous bronchial obstruction. Upper lobe tuberculous cavities with enlarged hilar nodes frequently mask roentgenological hilar or parenchymal shadows. Lower lobe infiltrates of recent development may be mistaken for recent bronchogenic spread of disease or caseous pneumonia.[6] Furthermore, a carcinomatous abscess may easily be mistaken roentgenologically for a tuberculous cavity. However certain definite clinical features should alert the physician to the possible presence of an associated neoplasm. Carcinoma should be suspected when there is persistent dull pain in the chest in the absence of pleural complications.[7] Likewise atypical changes appearing in serial chest films should direct attention to the possible presence of neoplasm. A profuse sudden hemoptysis occurring in a patient with limited tuberculosis is particularly apt to be caused by complicating carcinoma. Changes in the character of expectoration, progressive weight loss or marked anemia are of little help in diagnosis.

The coexistence of pulmonary tuberculosis and carcinoma of the lung may be expected to occur more frequently in the years to come as a result of frequent discovery of pulmonary tuberculosis in older people and increased incidence of primary pulmonary neoplasms. This should prompt physicians treating tuberculosis in older age groups to be more alert to the possible occurrence of the two diseases in the same patient.

As to the relationship of pulmonary tuberculosis and bronchogenic carcinoma, it is of interest to note that in this series of cases, the two diseases arose in different areas of the respiratory tract although they were found at autopsy to exist adjacently. Some writers are of the opinion that tuberculosis plays a small role, if any, in the production of primary carcinoma of the lung.[8]

SUMMARY

1) Five cases are reported in which active pulmonary tuberculosis was found in association with bronchogenic carcinoma.

2) The diagnosis of bronchogenic carcinoma in tuberculous patients is often difficult because the two diseases have many features in common.

3) The following clinical features have been helpful in the diagnosis of the coexistence of the two diseases: (a) Chest pain in the absence of pleurisy or other obvious cause. (b) Profuse, recurring hemoptysis which often occurs as a terminal event. (c) The appearance of an atypical shadow or shadows in serial chest films not in keeping with progressive tuberculosis.

4) Whenever atypical findings are present in a tuberculous patient of the middle or older age group, bronchoscopy and cytological studies of sputum and bronchial aspirated secretions are indicated to rule out complicating carcinoma.

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RESUMEN

1) Se relatan cinco casos en los que se encontró la asociación de tuberculosis y carcinoma bronquiogénico.

2) El diagnóstico de carcinoma bronquiogénico en los tuberculosos es a menudo difícil, porque las dos enfermedades tienen muchas características comunes.

3) Los siguientes datos clínicos han sido útiles para el diagnóstico de esa coexistencia: (a) Dolor torácico en ausencia de pleuresía o de otra causa justificada. (b) Hemoptisis recurrente que a menudo es el accidente terminal. (c) La aparición de una sombra atípica o en series de películas sin relación con la marcha del proceso tuberculoso.

4) Cuando hay hallazgos atípicos en un tuberculoso en edad madura o avanzada, la broncoscopia y los estudios citológicos del esputo y de las secreciones aspiradas, están indicados para descartar el carcinoma complicante.

RESUME

1) Les auteurs rapportent cinq cas dans lesquels s'associaient une tuberculose pulmonaire active et un cancer bronchique.

2) Le diagnostic de cancer chez les tuberculeux est souvent difficile à cause des nombreux éléments communs à ces deux affections.

3) Les constations cliniques suivantes furent d'un grand secours dans le diagnostic de la coexistence de ces deux affections: (a) Douleurs thoraciques en l'absence de pleurésie ou d'autre cause.

(b) Hémoptysie profuse et récidivante, que apparait souvent comme incident terminal. (c) Apparition sur les radiographies faites en série d'ombres atypiques qui ne paraissaient pas en rapport avec l'évolution tuberculeuse.

4) Chaque fois que des constatations atypiques sont faites chez un tuberculeux d'un âgé moyen, ou franchement âgé, on doit faire la bronchoscopie, l'examen cytologique des crachats, et des produits d'aspiration bronchique afin de déceler l'existence d'un cancer surajouté.

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Aneurysm of the Pulmonary Artery Due to Schistosomiasis*

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Schistosomiasis is an ancient and endemic disease in Egypt. It exists under two varieties: a haematobium and a mansoni. The worms of the former produce ova with a terminal spine which they deposit in the small veins of the urinary system, while in the latter the worms favor the intestinal tract and their ova have a lateral spine. S. mansoni is prevalent in the lower Nile Delta and is commonly attended with visceral complications in the liver, spleen and lungs, while S. haematobium is more frequent in the upper Nile Valley and its noted complications are mainly urinary.

The earliest clinical recognition of schistosomiasis of the cardio-pulmonary system was first reported by Azmy, Effat and Sorour in 1932, which disease they labelled Bilharzial Ayerza; later an extensive pathological study from the same school was conducted by Shaw and Ghareeb in 1938.

Though Schistosoma worms may reach the pulmonary artery or its branches and upon their death (accidentally or from antimony treatment) may follow a verminous dull congested lobular pneumonic allergic infiltrations, yet the usual picture is not due to the migrated worms but is due to the deposition of living ova in an around the terminal pulmonary arteriole. Schistosoma mansoni ova are particularly injurious, in that respect, especially to the vessels, though the incidence of schistosoma haematobium deposited ova may be higher in the lung.

There are two main forms of pulmonary schistosomiasis which are by no means individually separate; a cardiovascular and a parenchymatous, the one often merging into the other. The ova reach the lesser circulation either from the vesical veins in the schistosoma haematobium or across a porto-caval anastomosis in S. mansoni, the residence of which is confined to the portal tract. Only living ova are capable of exciting a histiocytic and a fibroblastic reaction in and around the arteriole, which they are capable of penetrating. They lie in its immediate vicinity causing an end-arteritis obliterans and the so-called bilharzial tubercle which is 0.5 to 1 mm. in diameter, greyish in color, firm in consistency

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and well fixed to its bed (Sorour). Microscopically, it is at first composed of histiocytes and esinophiles and later lymphocytes and giant cells. Gradually the tubercle is fibrosed and replaced by a nodular scar. Parenchymatous lesions are less frequent than the periarterial.

The deposition of the ova and the consequent train of events are patchy at first but the process gets more generalized as more and more ova reach the lung from the prolific schistosoma worms. The deposition favors the perihilar areas and peripherally the lower lobe than the upper, while the apices are noticeably free.

The bilharzial tubercle may end by calcification and this cause must be added to other known causes of calcified nodules in the lung. Histologically, the impacted ova in and around the arteriole show a necrotising arteriolitis with destruction of the media, that heals with obliterative endarteritis. The distinctive histological feature of the schistosomal pulmonary arteritis is the formation of angeiomatoids. The occluded vessel becomes canalized by new capillaries some of which dilate forming blood spaces lined by endothelium and in the absence of an intact medial coat this vascularized tissue expands beyond the normal boundaries of the vessel and may reach cavernous dimensions (Shaw and Ghareeb). There is also a process of obliterative endarteritis in the vasa vasorum of the big vessels (Sorour). These pathological processes lead to weakening of the arterial coat of the pulmonary vessels which begin to enlarge even in the absence of a constant rise of pressure either in the right ventricle or in the pulmonary artery.

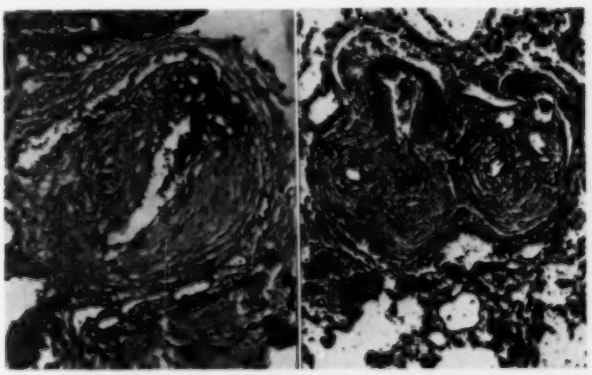

FIGURE 1 FIGURE 2

Figure 1: Impacted ova in a pulmonary vessel with obliteration of the lumen and marked histrocytic reaction and fibrosis.—*Figure 2:* Obliteration of the lumen and angeiomatoid formation.

Of 10 cases studied by Nasr Soliman in Cairo by means of cardiac catheterization there were only two that showed a distinct rise of pressure in the pulmonary artery, 74 and 47 mms. Hg. with the circulating pulmonary blood volume 1.6 and 0.8 litres respectively. Both cases showed aneurysmal dilatation of the main trunk and its branches. It seems probable that gross dilatation of the pulmonary artery is a late event partly due to local weakening of the vessel wall and partly to a rise of pressure as the process becomes increasingly generalized from repeated implantation of schistosoma ova. In ordinary emphysema the pressure in the pulmonary circuit may rise comparatively much higher yet the aneurysmal dilatation is lacking in spite of the secondary atheroma

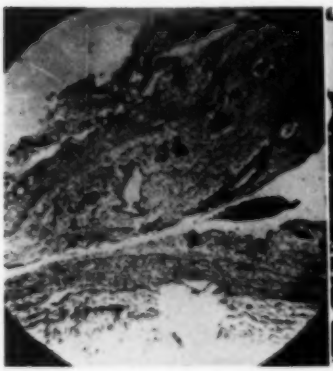

FIGURE 3
Ovum in vasovasoum.

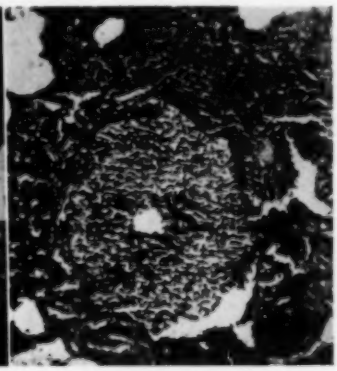

FIGURE 4
Bronchitis obliterans.

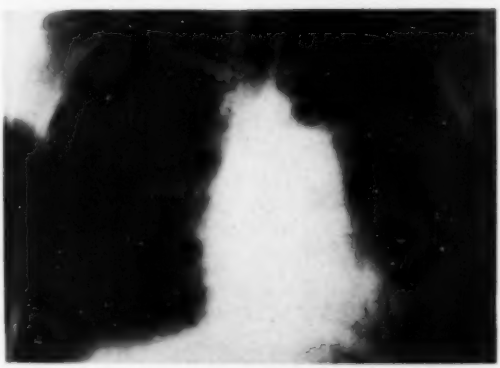

FIGURE 5a: Postero-anterior.

in the pulmonary artery. In atrial septal defect, in patent ductus arteriosus and in Roger's disease the gross enlargement encountered is due, besides the rise in pressure, to the increase of the circulatory blood volume in the pulmonary circuit.

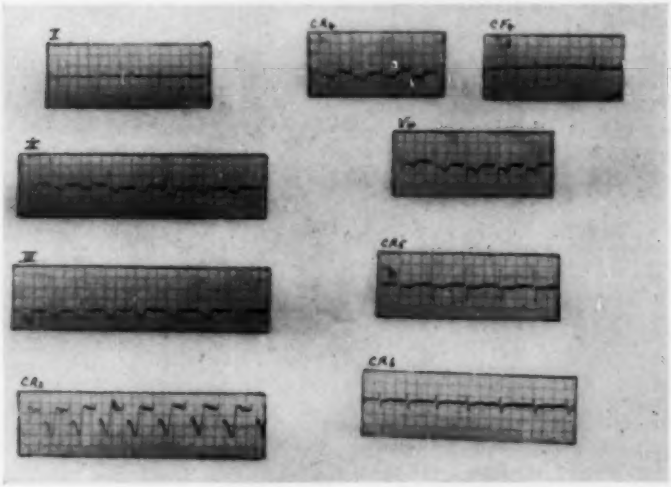

FIGURE 5b: Right ventricular enlargement and strain.

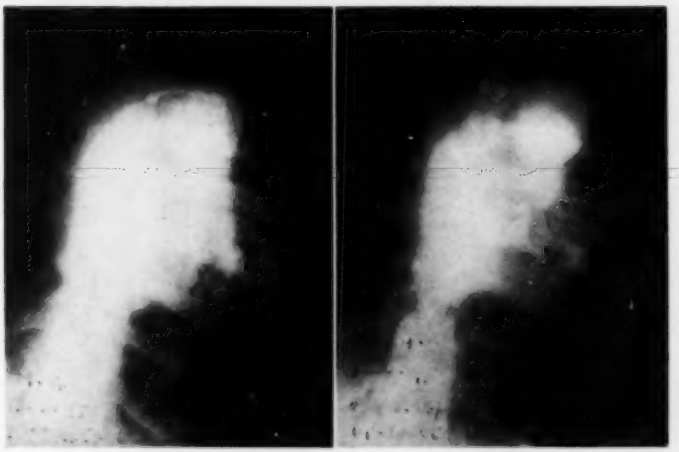

FIGURE 5c FIGURE 5d

Figure 5c: Two seconds after Diodrast.
Figure 5d: Four seconds after Diodrast.

FIGURE 6a FIGURE 6b FIGURE 6c

Figures 6a and 6b.: Four seconds after Diodrast (22/5/50). Large pulmonary artery and its branches—a diastolic pulmonary murmur and hilar dance. Diodrast.—*Figure 6c*: Digitalis and mercurials for 17 days (10/6/50).

Though Schistosoma ova have been reported in the myocardium, yet this rare event is in no way responsible for the schistosoma cor pulmonale. The hypertrophy and enlargement of the right ventricle are due to an increased strain on that chamber probably of various factors: (a) arteriovascular, (b) associated emphysema from schistosomal bronchiolitis obliterans (Sorour), (c) and the need to fill a widely dilated pulmonary artery and its branches.

We have had under our care in the past five years six instances of schistosomal aneurysm of the pulmonary artery. All of them were from the lower delta and had associated hepatomegaly and splenomegaly. The youngest was 14 and the oldest 55 years. Dys-

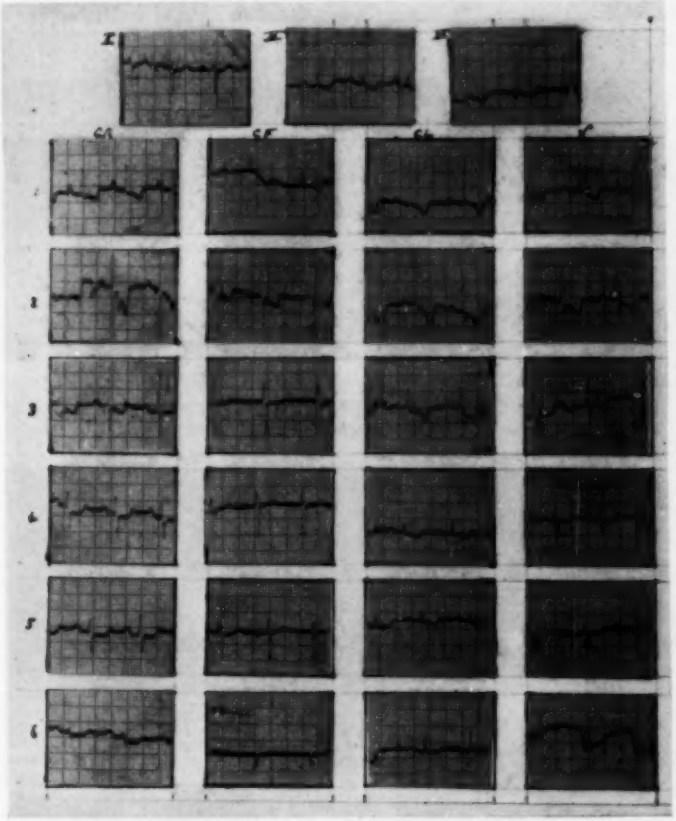

FIGURE 6d: Right ventricular enlargement and strain. Patient died suddenly after apparent improvement.

pnoea on slight exertion and cyanosis were present in all. Cyanosis is not an early feature in ordinary cases of vascular pulmonary schistosomiasis, but it is present when right cardiac strain develops. The presence of pulmonary aneursym is in itself an expression of an end result in a long series of events, in other words the last few strokes in a picture that took years to draw.

The neck veins were congested in all but the pulsations were vigorous, seen and felt in two, so much as to be mistaken for arterial at the first glance. The waves were throbbing synchronously with the ventricles. This means that in addition to an incompetent tricuspid valve there was an uninterrupted column of blood with a sufficiently tense venomotor tone as to be able to conduct a haemodynamic wave from the right ventricle across a distended right auricle without appreciable loss.

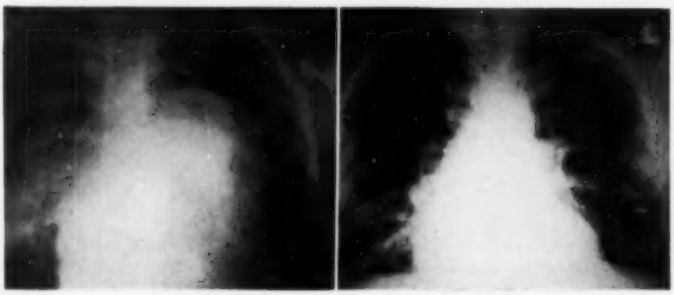

FIGURE 7 FIGURE 9

Figure 7: Four seconds after Diodrast.
Figure 9: More parenchymatous lesion than vascular.

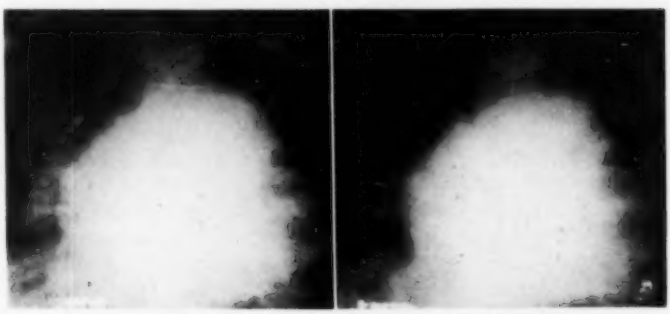

FIGURE 8a FIGURE 8b

Two seconds after Diodrast. Five seconds after Diodrast.

Diodrast and pericardial effusion associated; a boy of 14 years with pyelonephritis secondary to Schistosomiasis and B. coli.

Generalized oedema and ascites were present in all, probably due to a combination of: (a) hypoproteinoemia; from a poor protein diet, associated parasites as ankylostoma and ascaris, deficient albumin formation from a cirrhosed liver and excessive loss from bilharzial dysentry, haematuria or intestinal bleeding; (b) cardiac failure with venous congestion; (c) in one case there was ascending pyelonephritis secondary to bilharzial ureters.

Clubbing of the fingers was present in one case.

The chest showed the usual configuration seen in cases of schistosomal hepatosplenomegaly: conical, emphysematous, short in the vertical axis and with a wide everted subcostal angle. The heart was pushed upwards and placed horizontally, the apex frequently in the fourth interspace. The big vessels were likewise higher than normal. There was bulging and systolic pulsation in the second interspace, which in one case reached the midclavicular line laterally. The right border was one half to one inch outside the right sternal border. Auscultation showed besides haemodynamic systolic murmurs over the orifices, an accentuated second sound over the pulmonary in all, reduplication in one and diastolic murmur in two.

The electrocardiogram showed right ventricular preponderance and strain.

Radiography and angiocardiography disclosed a widened right ventricular cavity and conus, a diffuse aneurysmal enlargement and balooning of the pulmonary artery and its branches; the hilum standing out rigidly away from the mediastinum. Hilar dance was present along with a diastolic pulmonary murmur. There was no enlargement in the left auricle against the visualized esophagus but the pulmonary artery marked an indentation. A hypoplastic aorta suggests an atrial septal defect. The left ventricle showed moderate or slight enlargement. The cardiac surface area as well as the throbbing of the neck veins became appreciably smaller in two cases after mercurials and digitalis but the pulmonary vessels remained almost unchanged in size. The rest of the lung showed tortuous beaded vessels, pseudo-honeycombing and scattered hard nodular mottling more marked in the middle and lower zones; the whole engrafted on top of areas of increased transiucency due to localized or diffuse emphysema.

SUMMARY

Schistosomiasis exists in Egypt as: (a) Haematobium, mainly urinary and (b) Mansoni, mainly intestinal.

The lungs may be affected as follows:

1) Migration and death of the worms in the lungs leading to a verminous pneumonia (uncommon).

2) The deposition of carried living ova in terminal arteriole, Mansoni causing the most mischief. This leads to parenchymatous, bronchiolar and vascular changes. Endarteritis obliterans with angiomatoid formation and the development of the "bilharzial tubercle" are characteristic.

3) Aneurysmal dilatation of the pulmonary artery and its branches is a late manifestation probably due to a local weakening of the arterial coat from schistosoma ova deposit as well as associated malnutrition aided by increased pulmonary circulating blood volume and a gradual rise of blood pressure in the pulmonary circuit.

4) Dyspnoea is a constant feature in cardiopulmonary schistosomiasis, cyanosis signifies right ventricular strain and/or bronchiolar narrowing. The congested veins may conduct right ventricular pulsations. A pulmonary diastolic murmur may be heard.

5) The radiographic appearance shows enlargement of the right ventricle and the pulmonary artery, and its branches, beading and tortuous appearance of the small vessels. Pseudohoneycoming of the lung parenchyma and exaggerated bronchial shadows make the background.

6) The E.C.G. shows right ventricular hypertrophy with strain when failure sets in.

RESUMEN

La esquistosomiasis existe en Egipto como: (a) Hematobia, principalmente urinaria y (b) Mansoni, principalmente intestinal.

Los pulmones pueden afectarse como sigue:

1) Emigración y muerte de los gusanos en los pulmones conduciendo a una neumonía tóxica (poco común).

2) La detención de huevos vivos arrastrados por la corriente sanguínea hasta una arteriola pulmonar, este tipo Mansoni causando el daño mayor. Esto conduce a cambios parenquimatosos, bronquiolares y vasculares. Son características la endarteitis obliterante con formación angiomaitoide y el desarrollo de "tubérculos bilarzianos."

3) Dilatación aneurismal de la arteria pulmonar y de sus ramas como una manifestación tardía, probablemente debida a un debilitamiento local de la túnica arterial por los depósitos de huevos de esquistosoma asociada a desnutrición y a un aumento del volumen de sangre circulante y aumento gradual de la presión arterial en el circuito pulmonar.

4) La disnea es un síntoma constante en esquistosomiasis cardiopulmonar; la cianosis significa esfuerzo del centrículo derecho y/o estrechamiento bronquiolar. Las venas congestionadas pueden

conducir pulsaciones del ventriculo derecho. Un murmullo diastólico pulmonar puede auscultarse.

5) La apariencia radiológica muestra aumento del ventriculo derecho y de la arteria pulmonar y de sus ramas con apariencia de rosario o tortuosa de los vasos pequeños. Un aspecto falso de panel del parénquima pulmonar y sombras bronquiales exageradas pueden hallarse en el fondo.

6) El electro cardiograma muestra hipertrofia ventricular con esfuerzo cuando se establece la insuficiencia.

RESUME

La schistosomiase existe en Egypte sous forme: (a) de "Haematobium," le plus souvent à localisations urinaires, (b) sous forme de Mansoni, le plus souvent à localisations intestinales.

Les poumons peuvent être atteints de la façon suivante:

1) Migration et mort des vers dans les poumons menant à la constitution d'une pneumonie vermineuse (cas peu commun).

2) La plupart des troubles sont dus par la forme de Mansoni, lors du dépôt d'oeufs dans les artérioles terminales. Il en résulte des altérations parenchymateuses, bronchiolaires et vasculaires. Des oblitérations endartériennes, des formations angiomateuses et le développement de tubercules "bilharziens" sont caractéristiques.

3) La dilatation anévrysmale de l'artère pulmonaire et de ses branches réalise une manifestation tardive. Il est très probable que cet accident est dû à un affaiblissement local de la paroi artérielle à la suite du dépôt d'oeufs de schistosomes. Il s'y ajoute les troubles de la nutrition, favorisés par l'augmentation du volume du sang circulant, et l'élévation progressive de la pression sanguine dans la circulation pulmonaire.

4) La dyspnée est un facteur constant dans la schistosomiase cardiopulmonaire. Lorsqu'il y a cyanose, cela doit faire penser à l'existence d'une atteinte du ventricule droit ou d'un rétrécissement bronchiolaire. Les veines congestionnées peuvent être secouées par les pulsations du ventricule droit. On peut entendre un souffle diastolique à l'orifice pulmonaire.

5) La radiographie montre l'augmentation de volume du ventricule droit et de l'artère pulmonaire, ainsi que de ses branches. Les petits vaisseaux prennent un aspect moniliforme et sinueux. L'ensemble est caractérisé par un aspect du parenchyme pulmonaire simulant de multiples petites cavités et par une exagération des ombres bronchiques.

6) L'électrocardiogramme montre une hypertrophie du ventricule droit.

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Treatment of Broncho-Pulmonary Moniliasis by Dye Inhalation

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Often the picture of pulmonary mycosis is clinically indistinguishable from the clinical and roentgenologic manifestations produced by tuberculosis and certain primary neoplasms. If the sputum is negative for tubercle bacilli and no tumor can be demonstrated by biopsy or cytologic examination, the sputum should be examined for fungi. The following case clearly demonstrates some of the principles involved.

R.B., a 58 year old white female, entered the Jewish Consumptive Relief Society Sanatorium April 30, 1949. There was a 30 year history of pulmonary tuberculosis, during which time there had been numerous hospitalizations. On admission, her chief symptoms were incessant and distressing cough, weight loss, night sweats, and anorexia. Roentgenograms of the chest revealed a bilateral fibroid involvement extending, on the right, from the second anterior rib to the apex and, on the left, from the first anterior intercostal space to the apex (Figure 1). Twenty-eight consecutive sputum concentrates and cultures were negative when examined for tubercle bacilli. It was noted, however, that smears of her sputum contained a number of ovoid cells. In October 1949, a pure culture of Candida albicans was isolated from sputum cultured on Sabouraud's medium. The following clinical studies were made to rule out systemic moniliasis.

Renal: Urine specimens cultured for tubercle bacilli, pyogenic organisms, and fungi were negative. The phenolsulfonphthalein excretion test showed 25 per cent excretion in 30 minutes and 50 per cent in two hours. Intravenous urograms demonstrated poor excretory function in the left kidney. Cystoscopic examination showed moderate scalloping of the bladder neck with moderate trigonitis and urethritis. Ureteral catheters were passed to the renal pelves without difficulty.

Hepatic: Thymol turbidity—10.5 Maclagen units. Cephalin flocculation, negative in both 24 and 48 hours. Serum bilirubin, 0.8 milligrams per hundred cubic centimeters. There was 10 per cent bromsulfalein retention in 30 minutes when a dose of 5 milligrams per kilogram body weight was administered. Repeated attempts at cholecystography failed to visualize the gall bladder.

Cardiovascular: Electrocardiogram within normal limits.

Skeletal: Roentgenograms of ribs and the entire spine were negative.

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Gastrointestinal: Roentgenograms revealed an essentially normal digestive tract.

Miscellaneous: Skin tests with coccidioidin and histoplasmin were positive in 72 hours.

On October 28, 1949, a course of autogenous vaccine therapy was begun. The initial dose of 0.01 cc. given subcutaneously caused no reaction, and the dose was gradually increased until she was receiving 1 cc. twice weekly. On December 15, 1949, therapy with Lugol's solution was started, beginning with five drops three times a day and increasing by one drop per day. On January 5, 1950, symptoms of iodism developed and iodide therapy was discontinued. The in vitro sensitivity of the organism to several different antibiotics was then determined (Table I).

Treatment

The patient was given five courses of brilliant green aerosol inhalation therapy, each course 10 days long. At first 2 cc. of a 0.1 per cent solution were administered five times a day. In subsequent courses, the concentration was increased until a 0.3 per cent solution was used. No toxic effects were noted. There was a marked reduction in cough and sputum volume following the second course. The symptoms did not recur even though the therapy was interrupted. At the time of her discharge, November 15, 1950, she was still free of symptoms (Table II).

Discussion

Monilia is usually present as a saprophyte without producing any reaction in the host. Of the members of the genus Candida only one species, C. Albicans, is potentially pathogenic,[2] producing lesions in the mouth, vagina, skin, nails, bronchi or lungs, and occasionally causing septicemia, endocarditis or meningitis. Cas-

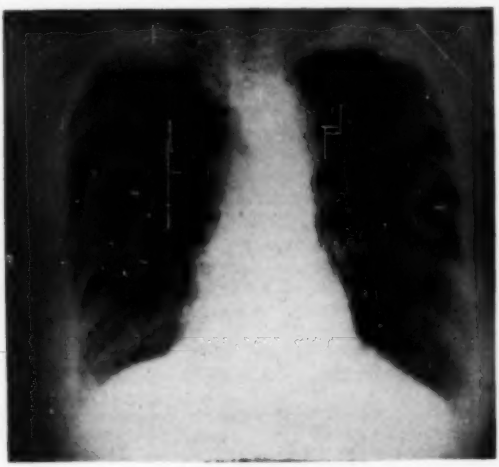

FIGURE 1

TABLE I

Antimicrobial Agent	Results
Penicillin	Organism grows in a concentration of 30 units per cc.
PAS	Organism grows in concentration of 10 micrograms per cc. of PAS.
Streptomycin	Organism grows in concentration of 100 micrograms per cc.
Potassium Iodide	Organism grows in 100 micrograms per cc. of potassium iodide.
Polymyxin Sulfate B N.D. 111*	Partial inhibition in a concentration of 6.25 micrograms per cc.; complete inhibition at 12.5 micrograms per cc.
Brilliant Green**	Complete inhibition in 0.2 micrograms per cc. or 1-5,000,000 concentration.

*Furnished by Burroughs, Wellcome and Company, Incorporated.

**Suggested by Dr. Henry Welch, Director, Division of Antibiotics, Food and Drug Administration.

TABLE II

Antimicrobial Agent	Results
3/17/50 0.1 per cent Brilliant Green	Direct smear of sputum showed many epithelial cells and many streptococci with fusiform organisms, but no fungi seen. Culture positive for C. albicans.
4/7/50 0.1 per cent Brilliant Green (with 0.2 gram streptomycin added to each inhalation)	Direct smear revealed mostly epithelial cells with moderate number of streptococci although much less than previous examination. Culture positive for C. albicans. *Marked improvement clinically. Decrease in cough and sputum.*
4/25/50 0.2 per cent Brilliant Green (with 250 mg. chloromycetin q.i.d. orally)	Direct smear showed no fungi. Occasional staphylococcus and streptococcus. Culture was positive for C. albicans.
5/24/50 0.3 per cent Brilliant Green	Direct smear showed moderate number streptococci, but no fungus. Culture showed no growth in 24 hours; some growth in 48 hours.
6/16/50 0.3 per cent Brilliant Green (with 250 mg. chloromycetin, q.i.d. orally)	There were no direct smear many plemorphic fungi which grew into yeast cell form in broth. The organism was found to grow in 25 micrograms of Brilliant Green inhibited in 50 micrograms per cc. Organism now 200 times more resistant. *Clinical improvement maintained.*
7/10/50 0.1 per cent Methylene Blue 11/15/50	Complete cessation of expectoration. Discharged; cough and expectoration still completely absent.

tellani's early description[3] of pulmonary moniliasis was that of a disease closely simulating tuberculosis in its clinical picture. Fever, weight loss, night sweats, fatigue, chest pains, cough, hemoptysis, dyspnea and anemia are usually present.

Primary infection in man is generally attributed to direct contact or inhalation.[4] In debilitated individuals, systemic infection may result from the extension of oral or cutaneous lesions. In each instance, it must be determined whether C. albicans is the primary cause of the disease or a secondary invader of some preexisting infection. A case report of systemic mycosis (moniliasis) in a drug addict[5] illustrates the necessity of considering the possibility of this syndrome whenever the clinical picture of subacute bacterial endocarditis cannot be confirmed by the demonstration of streptococcus viridans. Sutphin et al.[6] investigated the relationship, in five cases, (three siblings) between idiopathic hypoparathyroidism and moniliasis. No definite conclusions were drawn, but it was noted that the moniliasis preceded the hypoparathyroidism.

In the present case, the data suggest borderline hepatic involvement. The serum bilirubin and thymol turbidity are elevated; there is an increase in bromsulfalein retention. This, however, does not appear to be on the basis of systemic moniliasis. The failure of the gall bladder to visualize indicates that chronic cholecystopathy may be causing secondary hepatic dysfunction.

One should not use brilliant green in the treatment of fungus infection unless sure that the organism is sensitive to the dye in vitro. Studies in the presence of 25 per cent serum indicate a disparity between in vitro and in vivo sensitivity. Welch[1] found that "an organism classified as C. albicans was sensitive to brilliant green in a concentration of 1-6,000,000 for a 24 hour period. When tested over a period of 48 hours the effective concentration was 1-2,000,000. In the presence of 25 per cent serum, brilliant green was active against the organism in a concentration of 1-5,000 after 24 hours and 1-2,500 after 48 hours." He surmised that we would need a concentration of 1-100,000 in our case, but the in vivo concentration required was actually much greater.

It is possible that a more pronounced fungicidal effect could have been obtained if a greater concentration of dye had been used. The dye concentration, however, was limited by the fact that solutions of brilliant green with a concentration greater than 0.3 per cent had a tendency to clog the nebulizer. Achieving a higher systemic brilliant green level would thus involve either "dust inhalation" or intravenous administration. Stoval and Greely[7] have recommended intravenous gentian violet in the treatment of pulmonary moniliasis. Our patient showed satisfactory response

to methylene blue inhalation after the fungus had become resistant to brilliant green. In some cases, inhalation of gentian violet or malachite green would probably prove effective.

Streptomycin and chloromycetin were used as adjuvant therapy because a penicillin-resistant streptococcus was found in the sputum. Polymyxin B sulfate was not used because the necessary blood concentration of 6.25 to 12.5 micrograms would be inordinately high in view of the nephrotoxic properties of polymyxin.

SUMMARY

Pulmonary moniliasis, like tuberculosis, manifests itself in many ways, and does not necessarily respond to any one type of therapy. This case is presented because the gratifying clinical response to treatment suggests that brilliant green or compounds of similar structure can be of clinical value if properly used.

RESUMEN

La moniliasis pulmonar como la tuberculosis se manifiesta de varios modos y no responde obligadamente a tipo alguno de tratamiento. Se presenta este caso porque la satisfactoria respuesta clínica al tratamiento sugiere que el verde brillante o los compuestos de estructura similar pueden ser de valor si son usados adecuadamente.

RESUME

La moniliase pulmonaire, comme la tuberculose, a des manifestations variables, et ne répond pas nécessairement à un traitement univoque. Les auteurs rapportent cette observation parce que les résultats cliniques favorables qu'ils ont obtenus grâce au traitement suggèrent que le vert brillant ou des composés de structure analogue peuvent avoir une valeur clinique, si l'on en use convenablement.

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The Effect of Mecholyl on the Vital Capacity of Patients with Endobronchial Tuberculosis

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In a previous publication,[1] the question was raised whether bronchial lesions might not act as irritable foci to produce bronchospasm in persons previously free of asthma, or to potentiate bronchospasm in persons subject to asthma. That such reflex bronchial obstruction may occur was indicated experimentally by Binet and Burstein.[2] They prepared dogs with tracheotomy tubes so as to shunt off the lower tracheobronchial tree from the upper respiratory passages. In such animals, breathing through the tracheotomy tubes, passage of ammonia gas into the nose alone produced marked decrease in respiratory excursions, interpreted as bronchospasm. This reaction was relieved by sectioning the vagi. Even in dogs whose vagi were already severed, inhalation of ammonia fumes into the trachea led to bronchospasm, relieved by epinephrine. To explain this, a local irritant action with release of a chemical mediator acting on the bronchial walls to produce spasm was postulated. Finally, inhalation of the acetyl choline derivative carbamylcholine produced bronchospasm, which effect was potentiated if acid vapors were inhaled which in themselves had previously not been able to produce constriction of the bronchial tree.

In an effort to adduce information on these points, 11 patients with active pulmonary tuberculosis and various complicating tuberculous lesions in the bronchial tree, proved by bronchoscopic examination, were administered mecholyl* deeply subcutaneously. These subjects were free of asthma, as far as could be determined by careful history and observation in the course of their hospital stay. The effect of the drug on the vital capacity was measured at short intervals after the injection, using a Sanborn basal metabolism apparatus. The dosage was for the most part 10 mgm., which produced brisk side reactions of salivation, sweating, flush of face and upper parts of the body, and tachycardia, in varying degrees in all patients. The results are outlined in Table I. As is obvious, no profound change was produced in the baseline vital capacity of any of these patients, the maximum being a decrease of 23 per cent in one subject after a dose of 20 mgm.

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Acetyl Choline And Its Ester Mecholyl

Mecholyl is acetyl-beta-methyl choline chloride, a stable ester of acetyl choline. The latter is, with more or less unanimity of opinion,[3,4] held to be the chemical mediator of impulses at the parasympathetic postganglionic synapses ("muscarine-like action"), and likewise mediates impulses at all autonomic preganglionic synapses and also at motor nerve-muscle synapses ("nicotine-like action"). In the doses used in experiments such as ours, the action is mainly muscarinic, and can be abolished by atropine.

Opposing the action of endogenously formed and exogenously introduced acetyl choline and its homologues are circulating cholinesterases and cholinesterases *in situ*, guarding the various synapses where acetyl choline mediates nervous impulses. The human body can tolerate large intravenous doses of acetyl choline if given slowly enough,[5,6] as much as 0.09 to 0.14 gm. per minute, presumably because of rapid destruction of the drug by circulating cholinesterase.

Because the action of acetyl choline is on such varied nervous pathways, divergences of dosage and in the state of the organism tested can be expected to influence the results observed. This will be brought out in the following discussion. Even in the pharmacological laboratory disagreement as to the effect of acetyl choline on the dog's respiration is apparent, Koppanyi[3] reporting small effect, and Comroe and Starr[7] reporting definite bronchoconstriction. Possibly differences in methods account for such divergences of opinion.

In clinical experiments, in the dosage range commonly used, the action of mecholyl on the cardiovascular system is of utmost importance, since pulmonary vascular congestion may be reflected as a decrease in vital capacity, with which much of the following discussion deals. Ellis and Weiss[6] found little effect on the blood pressure or cardiac output in man when the drug was given slowly intravenously. Others have reported attacks of auricular fibrillation and cardiac standstill.[8,9] No reports of left ventricular failure or pulmonary edema have been found.

The nicotine-like action of acetyl choline on the muscles of respiration and on the respiratory center in the central nervous system apparently comes into play only after massive doses of the drug,[7] and is not a factor in the following clinical experiments.

The Action of Mecholyl in Asthmatics

The production by mecholyl of asthmatiform symptoms in patients who are subject to asthma is well documented, and has been attributed to bronchospasm.[5-7,10-14,19] This reaction has been uti-

TABLE I

Patient	Mecholyl Dosage (mgm.)	Control Vital Capacity (averages)	Interval Vital Capacities (averages)				Maximum Per cent Change	Bronchial Lesions
S.G., 42 male			1′	3′	5′	6′		Ulcerations, trachea and LMB*
	6	2450	2200	2200	2200	2200	10	
			2′	4′	5′			
	10	2450	2300	2400	2400		6	
			2′	4′	5′			
	16	2480	2330	2420	2400		6	
D.B., 37 female			1′	3′	5′			Ulcers and granulations, RMB*
	10	1200	1000	980	1000		18	
K.H., 25 female			2′	4′	5′	6′		Ulcero-granular RUL* orifice. (Allergic rhinitis)
	10	2620	2500	2400	2600	2250	14	
			1′	3′		6′		
	20	2410	2250	2380		2330	6	
N.C., 26 female			2′	4′	7′	10′		Ulcero-granular LMB* (History of asthma and allergic rhinitis)
	10	1300	1100	1100	1100	1200	15	
S.S., 44 male			1′	3′	7′			Ulcers and granulations, trachea and RMB*
	10	1660	1660	1460	1600		12	

Patient	Mecholyl Dosage (mgm.)	Control Vital Capacity (averages)	— — — Interval Vital Capacities (averages) — — —	Maximum Per cent Change	Bronchial Lesions
B.H., 28 female	10	1800	2′ 1660 / 5′ 1800 / 10′ 1700	7	Stenosis, LMB* (Allergic rhinitis)
C.B., 27 female	10	2040	2′ 1950 / 4′ 1900 / 8′ 1950	6	Ulcero-granular, RMB*
M.S., 40 female	10	1875	2′ 1800 / 4′ 1875 / 7′ 1800	4	Stenosis, RML* and RLL* orifices
C.P., 29 female	10	1200	2′ 1275 / 5′ 1300 / 10′ 1320	10 (incr.)	Stenosis and granulations, LMB*
J.V., 29 female	10	670	2′ 680 / 5′ 600	11	Stenosis LMB* Healed ulcers RMB*
N.O., 25 female	6	1750	2′ 1800 / 4′ 1700 / 5′ 1700	2	Ulcers and stenosis, LMB*
	10	1950	1′ 1700 / 3′ 1750 / 5′ 1700 / 7′ 1750	12	
	20	2150	2′ 2075 / 5′ 1650 / 7′ 1900 / 10′ 1950	23	

* LMB=left main bronchus. RMB=right main bronchus. RUL=right upper lobe.
RML=right middle lobe. RLL=right lower lobe.

lized in an elaborate series of clinical trials for evaluation of anti-asthmatic medications by Segal and his co-workers.[14-16] The drug is effective both by aerosol and parenteral routes. The degree of response, however, is variable, not only from patient to patient, but also in the same patient from time to time, varying directly with the amount of asthma the subject has recently had.[12,20] The dosage successfully used for such reactions has been 1 to 6 mgm. intramuscularly (Curry[12]), 10 to 20 mgm. subcutaneously (Moll[10]), 2.5 to 25 mgm. subcutaneously (Comroe and Starr[7]), 0.05 to 0.4 mgm. intravenously (Segal et al.[15]). Response by the intramuscular route was noted in two minutes by Curry, and in five to 10 minutes after subcutaneous administration by Moll. Using mecholyl intravenously, Segal noted typical responses within one minute. Anything less than a drop of 1 to 2 liters in vital capacity was not considered significant by Segal et al.[15] None of Curry's 16 patients with moderately active asthma responded with less than 18 per cent decrease in vital capacity.[12]

The action of the drug in these cases is muscarinic, for it can be abolished by atropine. The action of mecholyl is local in the bronchial tree, as proved by the effect obtained by aerosolization without systemic reactions.[14-16]

The Action of Mecholyl on Normal Human Subjects

Normal non-asthmatic subjects do not respond to acetyl choline or any of its derivatives with notable wheezing or dyspnea, according to most authors. Repeatedly it has been shown that normal persons at most complain only of substernal constriction, cough, or slight dyspnea, although the side effects of flush, sweating, etc., are as marked as in asthmatics.[5-7] Curry[12] found in 10 normal control patients a 6 per cent decrease as the maximum response; and in 11 patients with hay fever but without asthma the greatest response was 10 per cent decrease. Using a comparatively huge dose of 30 mgm. intramuscularly, Hurtado and Kaltreider[17] produced a fall of vital capacity in two normal subjects of 860 cc. and 700 cc. respectively, which exceed the effects in normal subjects reported by other authors. Also using a large dosage, 5 per cent carbaminoyl choline by inhalation, Dautrebande and Phillipot[22] produced bronchospasm in an unmentioned number of normal subjects. With 1 per cent acetyl choline aerosol, Tiffeneau and Beauvallet[21] and Gerrits[23] produced no effect in normals.

The Effect of Mecholyl on Patients with Pulmonary Disease Other Than Asthma

This aspect has been touched upon only briefly in the literature. Fraser[4] reported that in one patient recovering from pneumonia

but free of asthma, 25 mgm. mecholyl intramuscularly produced narrowing of the smaller bronchi as outlined by lipiodol. Tiffeneau and Beauvallet[11,21] reported that in silicosis, fibrous tuberculosis, and emphysema, a decreased vital capacity could be produced by mecholyl. André[18] did not share the enthusiasm of Tiffeneau and Beauvallet for the use of acetyl choline as a means of producing objectively recognizable effects in silicotics. Gerrits[23] produced bronchospasm in silicotics with 1 per cent acetyl choline aerosol. Curry[12] stated that in one patient with chronic non-allergic bronchitis mecholyl produced a marked decrease in vital capacity. Moll[10] found that three patients with pulmonary tuberculosis did not react to mecholyl with asthma, although three patients with bronchiectasis (2 with associated asthma) so reacted.

Discussion

If mecholyl produces bronchospasm, two challenging questions arise: Why do not all subjects respond to acetyl choline as asthmatics do? Is asthma a vagospastic phenomenon, due to endogenously liberated acetyl choline?

In answer to the first question, Moll[10] has postulated that an irritable damaged bronchial tree is necessary for the asthmatic response. "Given an irritable bronchus, it is conceivable how asthma may be provoked by certain allergic, reflex, and psychic stimuli which usually have no effect on normal subjects."[10] The cause of the irritability of the bronchial tree may be preceding respiratory infection or may be obscure, according to Moll.

The second question has been extensively debated. The attacks produced by mecholyl in every way simulate those of natural asthma, except that atropine will prevent or abolish the induced attack, whereas clinically atropine has not been notably effective. Dale and Gaddum[20] have suggested that such paradoxes may be explained satisfactorily by postulating that in the animal body, acetyl choline may be liberated too close to the effector organ to be effectively blocked by exogenously introduced atropine. Further knowledge on this point has not yet come from the reports of the action of the newer anticholinesterase insecticides in man.[24,25] In subjects poisoned with these agents, constriction of the chest and cough are common symptoms, but apparently more severe asthma-like manifestations have not occurred.

The failure to produce significant changes in the vital capacity in this series of patients with endobronchial tuberculosis, at least by the methods used, leads to the impression that more than an "irritable bronchus" is needed to respond with asthma-like symptoms to mecholyl. Furthermore, since an asthmatic background is apparently required, the mechanism of asthma production appar-

ently involves more than the separate or combined actions of acetyl choline and bronchial disease.

SUMMARY

The effect of mecholyl on the vital capacity of tuberculous patients with various endobronchial tuberculous lesions is not significant, as compared to the effect of this drug on asthmatics.

The possible light this sheds on the pathogenesis of asthma is discussed.

RESUMEN

El efecto del mecolil sobre la capacidad vital de los tuberculosos con diversas lesiones endobrónquicas no es importante comparado con el efecto de esta droga en los asmáticos.

Se discute la luz que esto proyecta sobre la patogenia del asma.

RESUME

L'effet du "mécholyl" sur la capacité vitale des bacillaires atteints de diverses lésions de tuberculose bronchique n'est pas une action aussi significative que celle du même produit sur les asthmatiques. Les auteurs discutent à la lumière que ces constatations peuvent apporter, la pathogénie de l'asthme.

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Plasma Cell Tumors of the Lung
Report of a Case

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To our knowledge the instance of solitary plasmocytoma of the lung herein reported is the third such case in the literature. Gordon and Walker[1] noted a solitary plasmocytoma in the left mid-lung field of a 30 year old white female. Stewart, in a personal communication to Gordon and Walker, described examples of solitary plasma cell tumor of the lung. Childress and Adie[2] recently reported one case of solitary plasmocytoma of the lung and another of the pleura, both of which were treated by surgical resection.

Hellwig,[3] in a thorough review of the literature up to 1943, found 128 examples of extramedullary plasma cell tumors; 110 of these were located in the air passages and conjuntiva. Bross,[4] cited by Hellwig, reported a case in the mediastinum. Klose[5] described an instance in the pleura. The nature of plasma cell tumors is not clearly established. They may be of malignant origin or they may represent a secondary granulomatous reaction due to chronic inflammation. Willis[6] noted that 25 per cent of solitary plasma cell tumors in soft tissues consist of metastases from the liver; this possibility must be considered and a careful evaluation made after the presence of such a lesion is detected. In most instances, however, the tumor is benign and grows slowly.

Case Report

A 57-year old white female secretary first visited our office on August 10, 1949, after a roentgenogram made during a chest x-ray survey of schools had revealed a solitary lesion in the left mid-lung field. Careful search for acid-fast bacilli had proved negative.

Past medical history included pneumonia in 1944, and a "pleurisy attack" in 1936. In February 1948, she experienced a sudden episode of severe pain in the chest which was relieved by lying down and vanished suddenly. She also complained of arthritis for many years for which she took iodine drops; the arthritic pains disappeared after lobectomy.

Physical examination on August 10 was essentially negative. Blood pressure was 138 systolic and 72 diastolic. Blood picture revealed hemoglobin 13.2 Gm.; red cells 4,000,000; color index 0.99, and leukocytes 7,700. The rare finding of polychromatophilia was present. Urinalysis was negative.

Bronchoscopy on August 25, 1949 revealed an extrinsic pressure on the lateral portion of the left main bronchus at the level and just below the

orifice of the left upper lobe. Exploratory thoracotomy was performed on August 29, 1949. A hard tumor about the size of a large lemon was found in the left upper lobe, in such a position that a segmental lobectomy could not be done. Many lymph nodes were seen in the hilum; a biopsy specimen from this area was negative for malignancy. A presumable diagnosis of hamartoma was then made and a left upper lobectomy carried out.

After removal, the lobe was sent to the pathologist for a frozen section; the report indicated an inflammatory disease. The pathologist's report read: the upper lobe of the left lung measuring 15 x 8 x 5.5 cm. in greatest dimensions and weighing 143 grams was received. The lobe has been amputated at the hilus just beyond the bifurcation of the bronchus leading to this lobe. In the central portion of the lobe and beginning

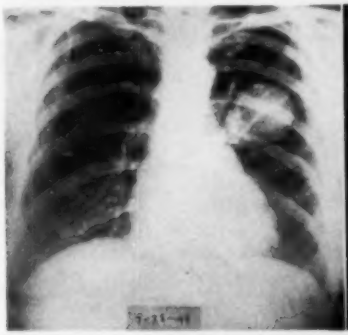


FIGURE 1

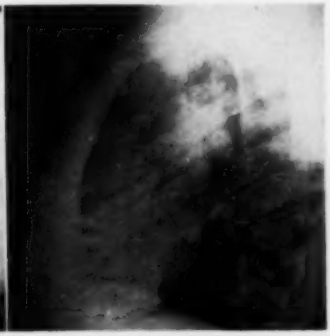


FIGURE 2

Figure 1: Pre-operative film showing tumor mass in left mid-lung field.
Figure 2: Lateral view showing tumor mass to be located close to left hilum.

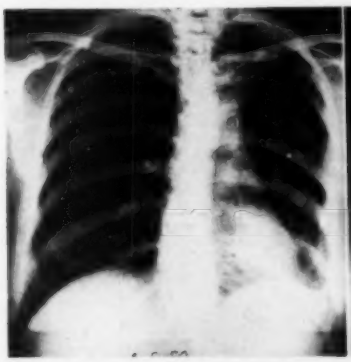


FIGURE 3

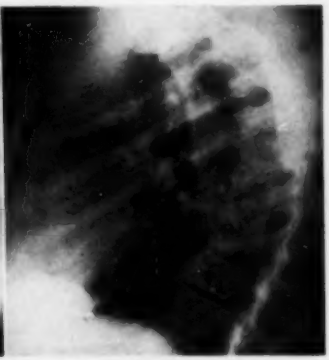


FIGURE 4

Figure 3: Post-operative film. Left lower lobe has completely re-expanded, filling the left chest.—*Figure 4:* Post-operative left lateral view.

within 1 to 2 mm. of its point of amputation there is a moderately firm, well circumscribed nodule fully 5 cm. in diameter. The cut surface shows it to be composed of homogeneous, pink-gray, somewhat rubbery tissue which in some areas has a slight yellow tinge. The mass lies between the bronchus leading to the upper portion of the lobe and the bronchus leading to the base. No connection with the bronchus can be demonstrated, but an artery fully 2.5 mm. in diameter leads into the mass.

Microscopic sections of the mass in the lung show, in the central part particularly, very dense fibrosis and numerous broad strands of almost hyaline connective tissue, in between which small areas are present, in

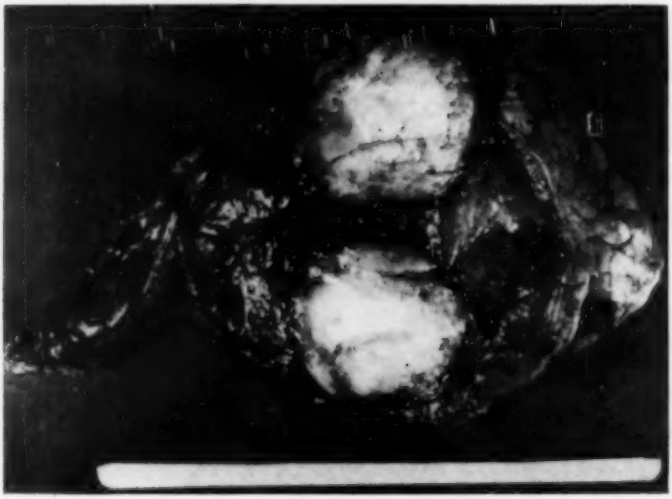
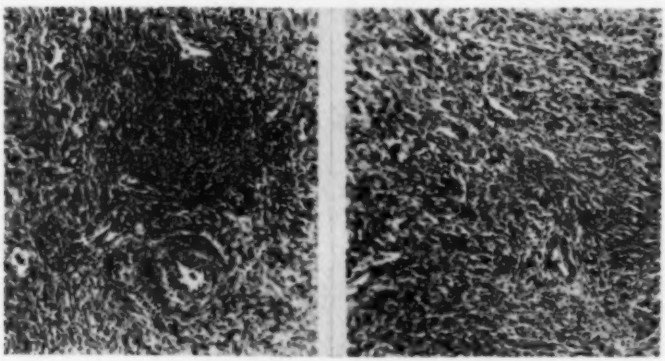


Figure 5: Operative specimen, left upper lobe, showing the tumor mass.



Microscopic Sections.

which one sees a few fusiform, swollen cells, apparently fibroblasts, mixed with which are a few round cells and occasional plasma cells. In other parts one sees also a few strands of dense connective tissue and other areas in which loose fibrous stroma is present. In this stroma one sees moderate numbers of fibroblasts, and in these parts particularly are fairly large numbers of lymphocytes and a few plasma cells. The architecture of the lung tissue is completely obliterated in these parts. At the border, where there is no capsule about the involved area, irregular patches of marked round cell infiltration are present, and there are a few young fibroblasts. In these peripheral portions one sees a few alveoli still remaining. Several distinct lymphoid foci are present, and some even show germinal centers. Slides were sent to Dr. F. Stewart of the Memorial Hospital, New York City, for further microscopic study, and the diagnosis of fibrosing plasmocytic granuloma of the lung was made.

The patient was last seen on April 5, 1951 and has resumed her normal secretarial activities. At present she is asymptomatic. Last x-ray film on April 5, 1951 showed no active disease.

SUMMARY

A case of solitary plasmocytoma of the lung is reported. Due to the frequency of malignancy in such tumors, the removal was warranted. Preoperative diagnosis of solitary plasma cell tumors of the lung is almost impossible. A careful search for other similar solitary extra-pulmonary tumors should be made, and the post-operative follow-up should be careful and prolonged.

RESUMEN

Se refiere un caso de plasmocitoma solitario. Debido a la frecuencia de la malignidad de estos tumores, la extirpación está justificada. El diagnóstico preoperatorio de estos tumores es casi imposible. Una cuidadosa búsqueda de otros tumores solitarios extrapulmonares debe hacerse y la observación postoperatoria debe ser acuciosa y prolongada.

RESUME

Les auteurs rapportent un cas de plasmocytose isolé du poumon. Etant donné la fréquence du caractère malin de cette sorte de tumeur, on décida d'en pratiquer l'exérèse. Le diagnostic préopératoire des tumeurs du poumon à plasmocytes est à peu près impossible. Il faut rechercher attentivement d'autres tumeurs similaires à localisations extra-pulmonaires et les soins post-opératoires doivent être assidus et prolongés.

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The Occurrence of Tubercle Bacilli in Spirometers Used by Patients with Pulmonary Tuberculosis*

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Spirometric and bronchospirometric studies are now done frequently on patients with pulmonary tuberculosis as well as on patients with non-tuberculous disease. Since two spirometers are necessary for doing bronchospirometry on one patient, four machines should be available if they are infected after their use by tuberculous patients and considered dangerous for non-tuberculous patients.

Stemmermann and Stern[1] tested a basal metabolism machine for tubercle bacilli. "After each of 14 patients with massively positive sputum had breathed and coughed into the machine for 10 minutes, the remaining gases were flushed out with air and the connecting rubber hoses were irrigated with saline. In not a single instance could tubercle bacilli be recovered from the washings, indicating that even after its continued use by highly 'positive' patients the basal metabolism machine is not a likely factor in the spread of pulmonary tuberculosis."

In spite of these findings the question of safety of using the same spirometers for tuberculous and non-tuberculous patients is frequently raised. It seemed, therefore, justified to do more extensive studies on the Benedict-Roth spirometers, which are used in many laboratories.

Method

Patients with active pulmonary tuberculosis with positive sputum were connected to the Benedict-Roth spirometers from one-half to three quarters of an hour during the routine examination of pulmonary functions. Included in these examinations were vital capacity determinations, during which the patient frequently coughed into the apparatus. Following the determination of vital capacity the maximum breathing capacity was examined. During this part of the test many patients coughed into the apparatus.

Immediately after the examination, the rubber mouthpiece was

*From the Pulmonary Physiology Laboratory, Halloran Veterans Administration Hospital, Staten Island, New York.

Sponsored by Veterans Administration and published with approval of Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect opinion or policy of Veterans Administration.

removed and sterile swabs were used to swab the metal part of the mouthpiece. In all cases there was sufficient wet material present to completely wet the swab and to collect into the sterile tube from 0.5 to 1 cc. of wet material. A fresh sterile swab was then used to completely swab and collect the water of condensation that had collected at the end of the expiratory hose. This usually consisted of from 1 to 2 cc. of material.

The dried sputum found in the expiratory part of the metal valve was scraped at intervals of six months on three different occasions, and collected in sterile tubes.

The expiratory rubber hose was cut open and scraped and washed down with 10 to 20 cc. of sterile saline on two different occasions after the hose had been in use for six months.

The collected material was concentrated with an equal quantity of 4 per cent sodium hydroxide and incubated at 37 degrees C. for 30 minutes. Using 8 per cent hydrochloric acid it was then neutralized. The specimen was centrifuged for 20 minutes and the sediment planted on 2 to 3 Petragnani slants. The cultures were examined weekly for eight weeks for growth. In all instances smears of the sediment were examined directly for tubercle bacilli.

Results

Table I is a summary of the bacteriological studies. Examination of 11 specimens from the metal mouthpiece, of 11 specimens from the expiratory tube, of three scrapings from the valve and of two scrapings from the expiratory tube were done. All these examinations were negative for tubercle bacilli on smear and culture.

TABLE I

SUMMARY OF BACTERIOLOGICAL STUDIES OF THE BENEDICT-ROTH SPIROMETERS

Origin of Specimen	No. of Exams.	Smear	Culture
Metal Mouthpiece (swabs)	11	negative	negative
Expiratory Hose (swabs)	11	negative	negative
Metal Valve (scraping: 6 month collection)	3	negative	negative
Expiratory Hose (scraping: 6 month collection)	2	negative	negative

These findings are in accordance with those of Stemmermann and Stern.[1] On the basis of these observations the conclusion can be made that tuberculosis infection by using the same spirometers is extremely unlikely. There does not seem to be any danger in

using the same machines for examining tuberculous and non-tuberculous patients.

Acknowledgment: Thanks are expressed to Mrs. Helen Ehrhorn Nuzzo of the Laboratory Services for the bacteriological examinations.

SUMMARY

Various parts of Benedict-Roth spirometers which had been used by patients with active pulmonary tuberculosis, having tubercle bacilli in their sputa, were examined for the presence of tubercle bacilli. In 27 different specimens no tubercle bacilli were found on smear or culture. It appears safe to use the same machines for the testing of tuberculous and non-tuberculous patients.

RESUMEN

Varias partes de espirómetros de Benedict-Roth que se habían usado en enfermos con tuberculosis pulmonar activa, fueron examinados en busca de bacilos de la tuberculosis. En 27 diferentes especímenes no se encontró el bacilo en frotis o en cultivo. Parece que el uso de las mismas máquinas para enfermos tuberculosos y no tuberculosos no ofrece peligro.

RESUME

Les auteurs ont recherché la présence de bacilles de Koch dans les différentes parties des spiromètres de Benedict-Roth qui ont été utilisés par des malades atteints de tuberculose pulmonaire active, avec expectoration bacillifère. Dans 27 spécimens différents ils n'ont trouvé aucun bacille de Koch, ni à l'examen direct, ni après culture. Il parait donc que l'on peut sans danger utiliser les mêmes appareils pour l'étude des malades bacillaires et de ceux qui ne le sont pas.

REFERENCE

1 Stemmermann, M. S. and Stern, A.: "Tubercle Bacilli in the Metabolic Apparatus," *Am. Rev. Tuberc.*, 53:264, 1946.

Eighteenth Annual Meeting of the College

College Headquarters

The Eighteenth Annual Meeting of the American College of Chest Physicians will be held at the Congress Hotel, Chicago, Illinois, June 5 through 8, 1952. The Annual Session of the American Medical Association will take place June 9-13. Reservations at the Congress Hotel for the College meeting and the meeting of the American Medical Association may be made by writing directly to the hotel. It is advisable that reservations be made at once and that the American College of Chest Physicians meeting is mentioned in all requests for reservations.

The scientific program to be presented at the annual meeting is now in preparation. Dr. Harold G. Trimble, Oakland, California, is chairman of the Committee on Scientific Program, and the members serving with him are: Dr. Charles P. Bailey, Philadelphia, Pennsylvania; Dr. Louis L. Friedman, Birmingham, Alabama; Dr. Paul H. Holinger, Chicago, Illinois; Dr. W. Leonard Howard, Northville, Michigan; Dr. Edwin R. Levine, Chicago, Illinois; Dr. Herbert C. Maier, New York, N. Y.; Dr. Nathaniel E. Reich, Brooklyn, New York; Dr. Leo G. Rigler, Minneapolis, Minnesota; Dr. O. A. Sander, Milwaukee, Wisconsin; Dr. Maurice S. Segal, Boston, Massachusetts; and Dr. Arthur J. Vorwald, Saranac Lake, New York.

Dr. Rigler will be moderator for the X-Ray Symposium to be held on Saturday afternoon, June 7. Physicians who plan to attend the meeting are invited to submit interesting cases for the Symposium. These cases must be proven by biopsy, surgery or autopsy, and can cover any subject of interest in chest diseases. Please send a concise summary including the pertinent history, physical findings including laboratory work and the final pathological proof together with your x-ray films to Leo J. Rigler, M.D., Department of Radiology, University of Minnesota, The Medical School, Minneapolis 14, Minnesota.

Dr. Holinger is in charge of the motion picture session to be presented on Friday evening, June 6. Recently a Committee on Motion Pictures was appointed by the President of the College with Dr. Holinger as chairman. It has been announced that all films to be presented in the motion picture session at the annual meeting must be reviewed by the committee before acceptance. Physicians are invited to submit films for review to Dr. Paul H. Holinger, 700 North Michigan Avenue, Chicago 11, Illinois. The other members of the committee are Dr. Alfred Goldman, Beverly Hills, California; Dr. H. Corwin Hinshaw, San Fran-

cisco, California; Dr. David H. Waterman, Knoxville, Tennessee; and Dr. Francis Woods, Brookline, Massachusetts.

The popular round table sessions are planned for Friday, Saturday and Sunday, June 6, 7 and 8. Suggestions for subject matter, discussants and moderators are invited and may be forwarded to Dr. Edwin R. Levine, 109 North Wabash Avenue, Chicago, Illinois.

The oral and written examinations for Fellowship in the College will be given on Thursday, June 5, at the Congress Hotel. Candidates who are eligible to take the Fellowship examinations are requested to write to the Executive Offices of the College, 112 East Chestnut Street, Chicago 11, Illinois, in order that proper arrangements may be made.

The Annual Convocation of the College will be held on Saturday, June 7, at the Congress Hotel. Fellowship Certificates will be awarded to all new Fellows who have met the qualification for such membership.

On Thursday, June 5, all of the councils and committees of the College will hold meetings at the Congress Hotel. The Board of Regents and Board of Governors will also hold their annual meetings on that day.

XII Congress, International Union Against Tuberculosis

II International Congress on Diseases of the Chest

These two important world Congresses will be held in Rio de Janeiro, Brazil, August 24 through 30, 1952. Chest specialists from every part of the world will gather there to discuss, in many languages, the subject of greatest interest to them all—the health of the people of the world.

The scientific program will be divided into two sections. All subject matter pertaining to tuberculosis will be presented by the International Union Against Tuberculosis. Requests for places on the program, dealing with tuberculosis, should be mailed at once, together with all pertinent information, to Professor Etienne Bernard, Secretary General, International Union Against Tuberculosis, 47 Rue de Courcelles, Paris, France.

Physicians who wish to present papers on nontuberculous diseases of the chest, both heart and lung diseases, are invited to communicate with Dr. Andrew L. Banyai, Chairman, Council on International Affairs, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

The organization of the scientific program is now under way and those physicians who desire to present papers should send titles and abstracts of their material to the designated program chairman at once.

Professor Manoel de Abreu and Dr. Reginaldo Fernandes, President and General Secretary, respectively, of the Congresses, have announced that there will be adequate hotel rooms available in Rio de Janeiro for those who attend. The rates for hotel accommodations are approximately $6.00 to $15.00 single and $8.00 to $20.00 double; suites are also available. Accommodations may be had on either American or European Plan.

Physicians in countries other than the United States who wish to

Rio de Janeiro, Brazil

travel in groups should contact the Governors and Regents in their respective countries for further information.

Physicians in the United States and Canada who wish to travel in a group should write at once to the Executive Offices of the College in Chicago.

The round trip fare from New York City to Rio de Janeiro on Pan American World Airways System is $848.00, plus $10.00 surcharge each way. For $180.00 additional, the tour may be continued around South America with the following stops: Montevideo, Uruguay; Buenos Aires, Argentina; Santiago, Chile; Lima, Peru; Panama City, Panama; Miami, Florida; and New York City.

It is most desirable that arrangements for attending the Rio de Janeiro Congresses be made at once. Members of the College in all countries should write immediately to the Executive Offices of the College, 112 East Chestnut Street, Chicago 11, Illinois, outlining the type of tour in which they are interested. The staff at the Executive Offices will be pleased to assist in every way possible.

PHILADELPHIA POSTGRADUATE COURSE

The Fifth Annual Postgraduate Course in Diseases of the Chest sponsored by the Council on Postgraduate Medical Education of the American College of Chest Physicians and the Laennec Society of Philadelphia, will be presented at the Warwick Hotel, Philadelphia, Pennsylvania, March 24-28, 1952. A program covering heart and lung disease has been arranged. Dr. Chevalier L. Jackson, Philadelphia, is chairman of the postgraduate course committee. Tuition fee for the course is $50.00; registration is limited and applications will be accepted in the order in which they are received. Physicians interested in attending the postgraduate course are invited to communicate with the Executive Offices, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.

PROFESSOR SIRIO LENTINI RECEIVES COLLEGE ESSAY AWARD

Professor Sirio Lentini is shown receiving the College Essay Award from Professor A. Omodei Zorini, Governor of the College for Italy. Professor Lentini's mother, other relatives and friends attended the ceremony held at the Forlanini Institute, Rome, Italy, October 25, 1951.

College Essay Award

Dr. Eli H. Rubin, Bronx, New York, chairman of the Committee on College Essay, announced the winner of the College Essay Award at the Annual Presidents' Banquet held in Atlantic City, New Jersey, on Saturday, June 9, during the Seventeenth Annual Meeting of the College. The winner of the 1951 Award of $250.00 and a Certificate of Merit was Professor Sirio Lentini of the Department of Pathology, University of Rome, Italy. The title of the winning paper is "Tomography of the Posterior Pneumo-Mediastinum in the Diagnosis of Diseases of the Mediastinum," which will be published in a future issue of *Diseases of the Chest*.

At a ceremony presided over by Professor A. Omodei Zorini, Rome, Italy, Governor of the College, held at the "Sala del Consiglio" of the Forlanini Institute in Rome, October 25, 1951, Professor Lentini received the Award. Professor Lentini's parents and friends attended the ceremony, as well as Professor Giovanni L'Eltore, Professor Giusto Fegiz and other members of the College in Italy.

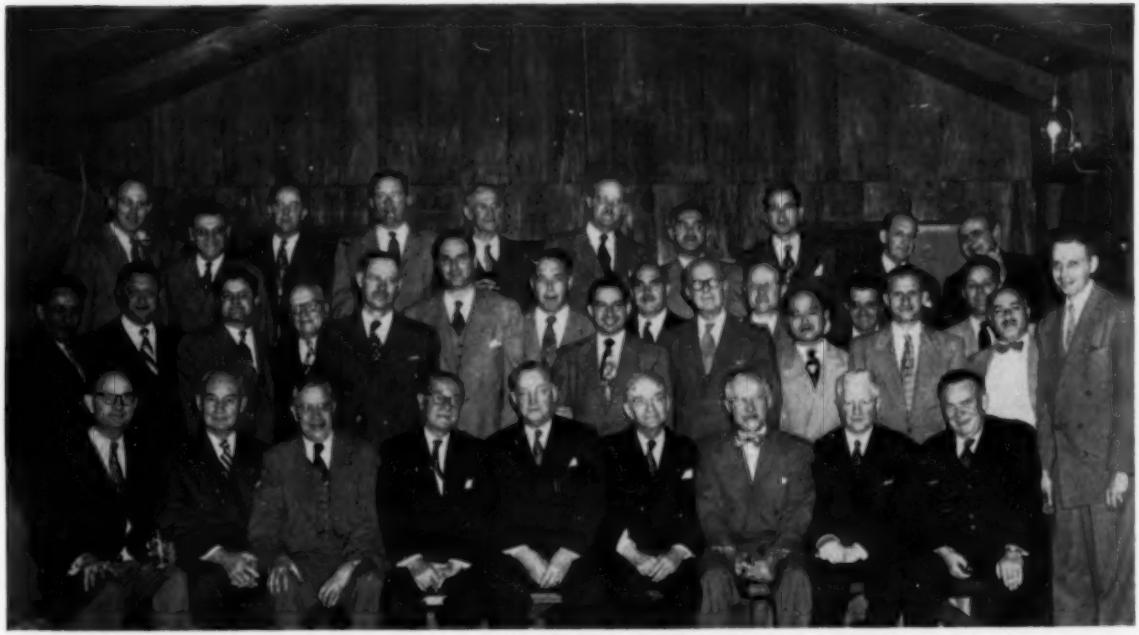
The 1952 College Essay Award will be made at the forthcoming annual meeting to be held in Chicago, Illinois, June 5 through 8, 1952. The contest is open to physicians in foreign countries as well as those residing in the United States, and all contributions must be submitted to the Executive Offices of the College in Chicago not later than April 1, 1952. Contributions must be original and may cover any phase relating to chest disease. The College reserves the right to invite the winner to present his contribution at the annual meeting and to publish the essay in *Diseases of the Chest*. Contestants are advised to study the format of the journal as to the length, form and arrangement of illustrations to guide them in the preparation of the manuscript. Five copies of the manuscript, typewritten in English, must be submitted; the only means of identification of the author or authors shall be a motto or other device on the title page and a sealed envelope, bearing the same motto on the outside, enclosing the name of the author or authors.

Dr. Henry C. Sweany, Tampa, Florida, is chairman of the committee for 1952, and the members serving with him are: Dr. E. Raymond Fenton, Washington, D. C.; Dr. Joseph S. Hiatt, McCain, North Carolina; Dr. Hugh L. Houston, Murray, Kentucky; and Dr. David Salkin, San Fernando, California.

COMMITTEE ON NOMINATIONS

Elections for offices expiring in June 1952 will be held at the Congress Hotel, Chicago, Illinois, on June 7. Recommendations for elective offices may be addressed to the chairman of the Committee on Nominations, Dr. Joseph C. Placak, 10515 Carnegie Avenue, Cleveland 6, Ohio. The other members of the committee are Captain Robert E. Duncan, Glendale, California and Dr. Robert E. Schwartz, Hattiesburg, Mississippi.

DINNER IN HONOR OF PAST PRESIDENTS AND REGENTS



Past Presidents, Regents and invited guests at a dinner given by Dr. and Mrs. Edward W. Hayes at their home in Monrovia, California, Saturday night, December 1, 1951.

Interim Session of the College

The Interim Session of the College was held at the Ambassador Hotel, Los Angeles, California, on Sunday, December 2, 1951. The California Chapter sponsored the session which included an excellent scientific program, round table luncheons, x-ray conference and a dinner. Over two hundred members and guests registered for the meeting. Dr. Jane Skillen, Olive View, President of the California Chapter, presided at the dinner on Sunday evening and introduced Dr. Leo Eloesser, the guest speaker. Dr. Edward W. Hayes, Monrovia, served as chairman of the General Arrangements Committee, Dr. Alfred Goldman, Beverly Hills, served as chairman of the Program Committee, and Dr. Louis I. Sokol was in charge of arrangements for the scientific assembly. They and their fellow committee members earned the congratulations of the officers and members of the College for the organization of a successful meeting.

The Past Presidents and Regents of the College were guests of honor at a cocktail party and buffet dinner given by Dr. and Mrs. Edward W. Hayes at their home in Monrovia, California, Saturday night, December 1, 1951. Approximately 100 physicians and their wives attended the dinner.

Minutes of the Semi-Annual Meeting Board of Regents

The semi-annual meeting of the Board of Regents of the College was held at the Ambassador Hotel, Los Angeles, California, on Monday, December 3, 1951. The meeting was called to order by Dr. James H. Stygall, chairman, at 2:00 p.m. The following officers, Regents and guests were present:

James H. Stygall, Indianapolis, Indiana, Chairman
Seymour M. Farber, San Francisco, California
Alfred Goldman, St. Louis, Missouri
Burgess L. Gordon, Philadelphia, Pennsylvania
Alvis E. Greer, Houston, Texas
Edward W. Hayes, Monrovia, California
Charles M. Hendricks, El Paso, Texas
William A. Hudson, Detroit, Michigan
Chevalier L. Jackson, Philadelphia, Pennsylvania
Hollis E. Johnson, Nashville, Tennessee
Louis Mark, Columbus, Ohio
Donald R. McKay, Buffalo, New York
Jay Arthur Myers, Minneapolis, Minnesota
James M. Odell, The Dalles, Oregon
J. Winthrop Peabody, Washington, D. C.
Charles K. Petter, Waukegan, Illinois
Joseph C. Placak, Cleveland, Ohio

Guests:

William A. Cassidy, Livermore, California
James S. Edlin, New York, New York
Alfred Goldman, Beverly Hills, California
James E. O'Malley, Anchorage, Alaska
David Salkin, San Fernando, California
Harold G. Trimble, Oakland, California

Murray Kornfeld, Chicago, Illinois, Executive Secretary
Harriet E. Lumm, Chicago, Illinois, Executive Assistant.

Dr. Charles K. Petter presented the report of the Treasurer of the College and the proposed budget for the year 1952. Motion was made by Dr. Mark for approval of the report, seconded by Dr. McKay and unanimously carried.

Dr. Petter then presented a resolution which had been prepared by a committee appointed by the President to consider the investment of surplus funds of the College. The committee on investments, consisting of Dr. Petter, chairman, Dr. Mark, Dr. Placak and Dr. Stygall, recommended the following:

> The Investment Department of the First National Bank of Chicago has recommended that at least part of the surplus funds of the College be used to purchase securities other than U. S. Defense Bonds, Series G; the College now holds $33,300 in these bonds paying 2½ per cent. Your committee recommends that between 25 and 30 per cent of surplus funds be invested in sound securities upon recommendation of the Investment Department of the First National Bank of Chicago. It is also recommended that the Executive Secretary investigate the advisability of investing another approximate 25 per cent of surplus funds in building and loan shares.

The above recommendation was moved for adoption by Dr. Hayes, seconded by Dr. Farber and unanimously carried.

Dr. Edward W. Hayes presented the report of the Council on Undergraduate Medical Education, of which he serves as chairman. The program is now under way, reported Dr. Hayes, to appoint committees in various cities that have medical schools, consisting of College members who are on the faculties. Personal contact by local members of the College interested in chest work in the medical schools is the most effective approach in stimulating improvement in the teaching of diseases of the chest.

In the absence of Dr. Andrew L. Banyai, Milwaukee, Wisconsin, chairman of the editorial board for the new book on nontuberculous diseases of the chest being published under the sponsorship of the College, Dr. Hayes reported that the first set of galley proofs for the book had been submitted to the authors, but because of the lateness in getting the material together, a tremendous amount of changes are being made in the original text. This has necessitated a complete revision of the present forms. A second set of galley proofs has now been received from the printer and upon approval of the revised proofs, page proofs will be submitted to Dr. Banyai. It is hoped that the book will soon be available.

The report of Dr. Hayes was approved upon motion of Dr. Hudson, seconded by Dr. Farber and unanimously carried.

The report of the Council on Postgraduate Medical Education was presented by the chairman, Dr. J. Winthrop Peabody. Dr. Peabody stated that eleven postgraduate courses in diseases of the chest were presented in various cities of the United States, as well as in Havana, Cuba and Manila, Philippine Islands, during the year 1951, and that more than 500 physicians attended these courses. Dr. Seymour M. Farber spoke briefly about the postgraduate course given in San Francisco and Dr. Chevalier L. Jackson described the successful course presented in Havana, Cuba.

Dr. Peabody announced that postgraduate courses planned to-date for 1952 would be held in Philadelphia, March 24-28, Chicago, October 6-10, and New York City, November 10-15. The first course sponsored by the College in 1952 was to be presented in San Francisco in January. Upon a motion by Dr. Mark, the report of Dr. Peabody was accepted with thanks, seconded by Dr. McKay and unanimously carried.

Dr. Peabody was then called upon to present the report of the Committee on Board Certification, of which he and Dr. John F. Briggs, St. Paul, Minnesota, serve as co-chairmen. Dr. Peabody maintained that there was still hope that a Certification Board on Diseases of the Chest would be established and that the committee would continue to make contacts and meet with appropriate groups in order to obtain such a board. Dr. Jackson moved the acceptance of Dr. Peabody's report, seconded by Dr. Farber and unanimously carried.

Dr. Chevalier L. Jackson, President of the College, reported that he had appointed the members for the newly established Committee on Bronchoesophagology. The committee chairman is Dr. Arthur M. Olsen, Rochester, Minnesota, and the members are Dr. Maurice Bonnier, Montreal, Canada; Dr. Arthur Cracovaner, New York City; Dr. Paul H. Holinger, Chicago, Illinois; Dr. Paul C. Samson, San Francisco, California; Dr. George McReynolds, Galveston, Texas; and Dr. Andre Soulas, Paris, France. The committee will serve under the Council on Management and Treatment of Diseases of the Chest and undertake such research problems that may be recommended by the Council. Dr. Jackson explained that other objectives of the committee would be to obtain outstanding papers on bronchoesophagology for presentation at the annual and international meetings of the College, thereby stimulating the interest of bronchoesophagologists in the College program.

The following resolution was read:

> WHEREAS It has been recommended that the councils and committees of the American College of Chest Physicians be streamlined to the fullest extent, and
>
> WHEREAS The Councils on Tuberculosis Committees, Tuberculosis Hospitals and Public Health, and the several committees serving under these councils have related activities, and
>
> WHEREAS The Councils on Research and the Management and Treatment of Diseases of the Chest, and the committees serving under these councils have related activities,
>
> THEREFORE BE IT RESOLVED That there be established a Council on Hospitals under which the various committees may serve, thereby abolishing the Councils on Tuberculosis Committees, Tuberculosis Hospitals and Public Health, and

BE IT FURTHER RESOLVED That the name of the Council on Management and Treatment of Diseases of the Chest be changed to the Council on Research and that all of the committees now serving under the present councils will serve under the newly established Council on Research, and

BE IT FURTHER RESOLVED That the by-laws of the American College of Chest Physicians be appropriately amended.

Motion was made by Dr. McKay, seconded by Dr. Hayes, that the resolution be approved and referred to the Committee on College By-Laws with instructions that the proposed changes be published in the College journal and submitted to the College membership at the next annual meeting (Article XIII, Amendments).

Dr. Alvis E. Greer presented a brief history of the newly organized Common Cold Foundation, which was formed by an amalgamation of the American Research and Education Foundation for Chest Disease and the Common Cold Institute. The Common Cold Foundation has been established for the purpose of conducting research on the common cold and other respiratory diseases. It is hoped that the Foundation will raise five million dollars from business and industry to further this objective. Dr. William A. Sawyer, Medical Consultant, Eastman Kodak Company, Rochester, New York, is the President of the Foundation, Dr. Charles M. Hendricks, El Paso, Texas, is Executive Director, and Dr. Andrew L. Banyai, Milwaukee, Wisconsin, is Associate Executive Director. Dr. Greer then read the following resolution:

WHEREAS There has been founded the Common Cold Foundation, a non-profit organization incorporated in the State of Illinois, for the purpose of raising funds to carry on research on the common cold, and

WHEREAS The American Research and Education Foundation for Chest Disease, which had been previously incorporated for this purpose, was endorsed by the American College of Chest Physicians, and

WHEREAS A number of officials of the American College of Chest Physicians are serving as directors and in other capacities with the Common Cold Foundation, and

WHEREAS This Foundation has been endorsed by the Industrial Medical Association,

THEREFORE BE IT RESOLVED That the American College of Chest Physicians endorse the Common Cold Foundation and lend its full support and cooperation to further its activities.

Upon motion by Dr. Mark, seconded by Dr. Placak, the resolution was unanimously adopted.

In the absence of Dr. Otto L. Bettag, Chicago, Illinois, Chairman of the Joint Committee on Chest X-Ray of the College and the American College of Radiology, Dr. Stygall read the report of the committee. In a communication from the Executive Secretary of the American College of Radiology it was stated that their Board of Chancellors were desirous of revising one section of the present report. Upon motion by Dr. Gordon, seconded by Dr. Goldman, the report was approved pending revision by the American College of Radiology.

Dr. Jay Arthur Myers, chairman of the Editorial Board of the College journal, *Diseases of the Chest*, presented a report in which he outlined the plans for the coming year, particularly stressing the importance of including papers on the subject of cardiovascular diseases. The report was accepted with thanks upon motion of Dr. Mark, seconded by Dr. Gordon.

Dr. Alvis E. Greer, chairman of the Board of Examiners, reported that 52 candidates for Fellowship in the College took their written and oral examinations at the annual meeting held in Atlantic City in June, 1951. Of the 52 physicians who took the oral and written examinations, 50 passed and will receive their Fellowship Certificates at the next annual Convocation of the College in Chicago. Dr. Greer discussed plans for improving the procedures in examining and grading candidates for Fellowship. Upon motion by Dr. Hayes, seconded by Dr. Peabody, the report was unanimously adopted.

Dr. Harold G. Trimble, chairman of the Committee on Scientific Program for the next annual meeting of the College, outlined the committee's plans for organizing one of the most outstanding heart and lung programs ever presented. Dr. Trimble's report was received with interest and unanimously approved upon motion by Dr. Hayes, seconded by Dr. Hudson.

Dr. Chevalier L. Jackson presented a report of the Council on International Affairs in the absence of Dr. Andrew L. Banyai, the chairman. Dr. Jackson announced that the Second International Congress on Diseases of the Chest, sponsored by the Council, will be held in Rio de Janeiro, Brazil, August 24 through 30, 1952, and will be held during the same week as the XII International Union Against Tuberculosis. The scientific program for both Congresses is now being organized and announcement was made that papers dealing with tuberculosis would be presented by the XII International Union Against Tuberculosis. Requests for places on this program are to be forwarded to Professor Etienne Bernard, the General Secretary of the International Union, 47 Rue de Courcelles, Paris, France. Physicians who wish to present papers on nontuberculous diseases of the chest are to communicate with Dr. Andrew L. Banyai, chairman of the Council on International Affairs of the College, 112 East Chestnut Street, Chicago 11, Illinois. The Board of Regents approved the report presented by Dr. Jackson and pledged their wholehearted support of the two world Congresses.

Dr. James S. Edlin, Secretary of the Committee on Resident Fellowships, reported that the program of this newly organized committee which was formed to help doctors in other countries to come to the United States for postgraduate study, was well under way. To date, the following Fellowships have been established: United Fruit Company Fellowship; S. H. Camp Company Fellowship; and Dr. Alfred A. Richman Fellowship. Dr. Edlin further reported that applications for Fellowships are now being received by the committee, and that all applications must be approved by the Governor and Regent of the College wherein the applicant resides. The report of the Resident Fellowship Committee was unanimously adopted by the Board.

A report of the Committee on Motion Pictures was read in the absence of the chairman, Dr. Paul H. Holinger of Chicago. One of the functions of this newly organized committee is to review new films on diseases of the chest for publication in the College journal. The second function is

to review films prior to their acceptance for presentation at College meetings. The committee will also strive to make good films available for teaching purposes in this country and abroad through the College chapters. Upon motion by Dr. Johnson, seconded by Dr. Odell, the report was approved.

In the absence of Dr. Otto L. Bettag, chairman of the Committee on Chest Diseases in Institutions, the report of that committee was read.

"The special survey by this Committee of all mental and penal setups in the United States and its possessions is still in progress. Mr. Murray Kornfeld, Executive Secretary of the College, conferred in Washington, D. C., with Robert J. Anderson, M.D., Chief, Division of Tuberculosis and Chronic Diseases, United States Public Health Service, and presented the Committee findings to date. As a result, negotiations are in progress for assigning a full-time medical officer of the United States Public Health Service to follow through in the establishment of proper facilities, etc., for the detection, isolation, treatment and eventual eradication of tuberculosis from mental and penal institutions in the United States and its possessions. The studies of this Committee have repeatedly pointed out the need for improvement in these centers.

"'Tuberculosis in Correctional Institutions—A Follow-up Study' was presented by one of the Committee members (O.L.B.) before the 81st Annual Congress of Correction on October 23, 1951 at Biloxi, Mississippi, the data in part having been obtained from the Committee files. This paper was discussed by Clarence Kooiker, M.D., Radiologist, United States Medical Center, Springfield, Missouri.

"The Medical Correctional Association is contacting the American Prison Association, the American Psychiatric Association, etc., in an effort to improve the mental and physical care of inmates, with special emphasis on tuberculosis."

Upon motion by Dr. Hudson, seconded by Dr. Farber, the report was unanimously approved.

The Board of Regents extended their thanks and appreciation to Dr. and Mrs. Edward W. Hayes for the lovely dinner party given at their home in Monrovia on Saturday evening, December 1. The party was given in honor of the Past-Presidents and members of the Board of Regents of the College, and approximately 100 guests attended. The Board also expressed their appreciation to Dr. Hayes and to Dr. Alfred Goldman and the members of the California Chapter for the excellent arrangements and interesting scientific program of the Interim Session of the College.

The Board of Regents expressed their sincere best wishes for a prompt and complete recovery to Dr. John F. Briggs, St. Paul, Minnesota, and to Dr. William R. Rumel, Salt Lake City, Utah, who were unable to attend the meeting because of illness.

The meeting was adjourned.

College Chapter News

SECOND NATIONAL MEETING OF BRAZILIAN CHAPTERS

The Brazilian Chapters of the College held a joint meeting at the Financial Hotel, Belo Horizonte, Minas Gerais State, October 5, 1951. On the Board that presided over the meeting we can see from left to right: Drs. A. Sefton; Paulo de Sousa Lima; Lourival de Mello Motta; Reginaldo Fernandes, Governor, Central Brazilian Chapter; Fernando Gomez, Regent, Uruguay; Orlando Cabral Motta, Governor, Minas Gerais Chapter; Jose Rosemberg, Governor, Southern Brazilian Chapter; Agenor de Sousa Bomfim; and Ernani Bettega.

URUGUAYAN CHAPTER

The Uruguayan Chapter of the College met at the Institute of Tuberculosis, Montevideo, Uruguay, December 14, 1951. Professor Fernando D. Gomez, Regent for Uruguay, spoke of plans for the XII Congress, International Union Against Tuberculosis and the II International Congress on Diseases of the Chest, to be held in Rio de Janeiro, Brazil, August 24-30, 1952. The following scientific program was presented:

"Dos casos de estenosis bronquial parcial tuberculosa con estudio angiocardioneumografico,"
Ricardo Rimini, Raul Burgos y Abelardo Rodriguez.

"Presentacion de casos radiologicos diversos (tumor neurogenetico, estrechez mitral, etc.),"
Nicolas Caubarrere.

"A proposito de una observacion de amiloidosis generalizada con comprobacion necropsica,"
Cleopatra Epifanio y Juan J. Scandroglio.

"Evolucion particular de un caso tratado con estreptomicina,"
Aristeo Piaggio.

Officers elected for the coming year were:
Nicolas Caubarrere, President,
Cleopatra Epifanio, Secretary-Treasurer.

Cleopatra Epifanio, Secretary.

NEW JERSEY CHAPTER

The New Jersey Chapter of the College will hold a meeting at the B. S. Pollak Hospital for Chest Diseases, Jersey City, February 26, 1952, at 8:15 p. m. The following program will be presented:

I. "Some Basic Effects of Cortisone as Related to Pulmonary Disease," David M. Spain, Pathologist, Department of Laboratories and Research, Westchester County, New York.

Discussors: 1) J. Earl Gerber, Pathologist, B. S. Pollak Hospital for Chest Diseases, Jersey City, New Jersey.

2) Louis Siltzbach, Attending Physician, Pulmonary Division, Montefiore Hospital, New York City, and Adjunct Physician, Pulmonary Service, Mt. Sinai Hospital, New York City.

II. "Segmental Resection in Pulmonary Tuberculosis—Experiences in 300 Cases,"
J. Maxwell Chamberlain, Associate in Surgery, Columbia University Medical School, and Associate Visiting Surgeon, Chest Service, Bellevue Hospital, New York City.

Discussors: 1) Frank Bortone, Chief Surgeon, B. S. Pollak Hospital for Chest Diseases, Jersey City, New Jersey.

2) Paul Geary, Thoracic Surgeon, Roosevelt Hospital, Glen Gardner and Bonnie Burns Sanatoria, New Jersey.

III. General Discussion.

IV. Collation.

Irving J. Selikoff, Secretary.

NEW YORK CHAPTER

The Twelfth Annual Clinical Meeting of the New York State Chapter of the College will be held at the Hotel New Yorker, February 21, 1952. There will be morning, luncheon, and afternoon sessions.

The Twelfth Annual Meeting of the New York State Chapter of the College will be held in conjunction with the Annual Meeting of the New York State Medical Society, May 15, 1952. The Second Annual Howard Lilienthal Lecture will be delivered by Dr. Andrew L. Banyai on "Therapeutic Application of Pneumoperitoneum."

Harry Golembe, Secretary.

PUERTO RICO CHAPTER

The Annual Meeting of the Puerto Rico Chapter of the College was held at the Insular Sanatorium, December 12, 1951. Papers were presented by Dr. Andrew L. Banyai, Milwaukee, Wisconsin; Dr. Richard Kern, Philadelphia, Pennsylvania; and Dr. J. M. Moscoso, Trujillo, Dominican Republic.

The following officers were elected for the coming year:

Eugenio Fernandez Cerra, Santurce, President,
Alicea Reinhardt, Rio Piedras, Vice-President,
Pedro J. Durand, Rio Piedras, Secretary-Treasurer.

Pedro J. Durand, Secretary.

College News Notes

The College News Section of *Diseases of the Chest* is devoted to the activities of the members. Kindly send all news items to the American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.

Dr. Luis Saye of Buenos Aires, Argentina, visited Havana, Cuba, in December 1951 and gave a series of lectures on tuberculosis under the auspices of the Ministry of Public Health at the Sociedad de Tisiologia.

Dr. Jorge Higgins, Guayaquil, Governor for Ecuador, attended the last session held in honor of Dr. Saye at the Sociedad de Tisiologia while en route to Haiti on a mission for the World Health Organization.

Dr. Edgar Mayer, New York City, presented a paper entitled "The More Recent Aspects of Chronic Pulmonary Diseases," at a meeting of the Montreal Clinical Society, November 28, 1951.

Dr. Horace DeLien, Director of Health Mission to the Philippine Government, Emergency Cooperative Administration (ECAO) Scientific and Technical Emergency Mission (STEM) will be spending the next two years in the Philippines on a special mission for the purpose of putting the program of the above agencies into full operation. Dr. DeLien will be guest speaker at the next meeting of the Philippine Chapter of the College.

Dr. Max Sadove, Oak Park, Head of the Department of Anesthesiology at the University of Illinois, was elected organizing president of the Walter Reed Society at the first official meeting of the group held in Los Angeles. The society which is sponsored by the National Society for Medical Research is comprised of those who have served as "human guinea pigs" in medical research or experimentation under the direction of a qualified scientist. Dr. Sadove has frequently been a "guinea pig" and has just recently conducted some dramatic experiments with 50 volunteers at the University of Illinois. These experiments dealt with artificial respiration studies conducted at the request of the Defense Department.

Dr. Otto L. Bettag, Chairman of the Committee on Chest Diseases in Institutions of the American College of Chest Physicians, presented a paper entitled "Tuberculosis in Correctional Institutions," at the Annual Meeting of the Medical Correctional Association in Biloxi, Mississippi, October 23, 1951. Dr. Bettag was elected Vice-President of the Medical Correctional Association at an election of officers held at the meeting.

A new motion picture film by Dr. Paul H. Holinger and Dr. Kenneth C. Johnston, Chicago, Illinois, entitled "The Endoscopic Appearance of Diseases of the Trachea" was shown at the annual meeting of the American College of Surgeons held in San Francisco, California, November 1951. The American College of Surgeons awarded the film a Certificate of Merit as the best teaching film reviewed by their committee in 1951.

CUBAN POSTGRADUATE COURSE

The Second Postgraduate Course on Diseases of the Chest sponsored by the Cuban Chapter of the College was presented at the Institute of Respiratory Disease, Hospital Calixto Garcia, Hospital Sanatorium "La Esperanza," and Hospital Ortopedico. Previous to the inauguration of the course, a discussion of the College and the Postgraduate Course was televised in which Dr. Sanchez Acosta, Dr. Arnaldo Core and Dr. Antonio Navarrete participated. For the first time in Cuba, the operations and demonstrations were televised over a local network.

ANNOUNCEMENTS

A course in Broncho-Esophagology will be given at Temple University, April 14-25, 1952. The fee is $250. For application blanks and further information please communicate with the Department of Broncho-Esophagology, Lab 604, 3400 N. Broad St., Philadelphia 40, Pennsylvania.

Chevalier Jackson and Chevalier L. Jackson.

COURSES IN LABORATORY DIAGNOSIS OF TUBERCULOSIS

In cooperation with the Division of Chronic Disease and Tuberculosis, Public Health Service, the Bacteriology Laboratories of the Communicable Disease Center, Chamblee, Georgia, will offer two courses in the laboratory diagnosis of tuberculosis on the following dates: May 19-23, 1952, and November 3-7, 1952.

Practical laboratory training in all phases of tuberculosis bacteriology, including preparation of culture media, microscopy, cultural procedures, diagnostic use of animals, and testing of drug sensitivity will be included in the course. No tuition or laboratory fees are charged. Reservations for the courses should be made well in advance.

Additional information and applications may be obtained from the Officer in Charge, Laboratory Training Services, Communicable Disease Center, Public Health Service, P. O. Box 185, Chamblee, Georgia.

BINDING FOR COMPLETED VOLUMES

We are pleased to announce that the Publishers Authorized Bindery Service, 308 West Randolph Street, Chicago, Illinois, will produce a well-bound volume at as low a price as possible for those members and subscribers who wish to preserve their issues of *Diseases of the Chest*. They will bind the six issues of Volume XX in the best grade of washable buckram with gold stamping on the spine and the member's or subscriber's name in gold on the front cover. Please send the six issues to Chicago, parcel post prepaid, with check or money order for $3.30 made payable to the Publishers Authorized Bindery Service. The bound volumes will be returned with transportation prepaid by the bindery.

Obituaries

HARRY SAMUEL ARKIN

1893 - 1951

Dr. Harry Samuel Arkin was born in 1893. He grew up in Chicago, took his pre-medical work at the University of Chicago and was graduated from Rush Medical College in 1917. He served his internship at Cook County Hospital. He was in the Medical Corps of the army during World War I, but the armistice was concluded before he was shipped overseas.

He practiced in Chicago during his entire professional career. Shortly after starting practice he became associated with Dr. Max Biesenthal when the latter was appointed as head of the Chicago Winfield Tuberculosis Sanitarium, and up to the time of his death was an interested and active practitioner in the treatment of tuberculosis. He was a member of the American Trudeau Society, and one of the founder members of the American College of Chest Physicians.

He affiliated himself with Northwestern Medical School and rose to the position of assistant professor. For many years he was attending man on the Staff of Cook County Hospital in internal medicine, and consultant at Hines Veterans Hospital. He was one of the founder members of the Michael Reese Hospital chest service, and held the position of attending medical physician at Michael Reese Hospital. He was a member of the Board of Internal Medicine. He was an active member of the various societies of Internal Medicine and Tuberculosis.

He died at the age of fifty-eight of a heart attack, having been actively engaged in practice almost to the date of his death. He is survived by his widow, Irene and his brother Dr. Aaron Arkin.

His ernest consciousness and his interest in his profession impressed his associates and friends. He worked hard all his life, from the time he helped put himself through Medical School by taking a steady job in the city health department plus a temporary job as a salesman at Marshall Field and Company, to the time that his first cardiac attack forced him to give up some of his activities. During his entire career, devoted to the practice of internal medicine, his chief interest lay in those conditons which had to do with pathology of the respiratory system.

Ralph B. Bettman and
Darrell H. Trumpe, Governor for Illinois.

ROBERT GRAHAM BELL

1886 - 1951

Dr. Robert Graham Bell of Ottawa, Illinois, passed away on July 28, 1951, at Billings Memorial Hospital, Chicago, Illinois, at the age of 65.

Dr. Bell was born June 7, 1886, at Ossian, Indiana. He received his preliminary education in the Ossian Public Schools and was a graduate of Wabash College at Crawfordsville, Indiana. He taught school for some time and entered Rush Medical College, Chicago, Illinois, where he graduated in medicine in 1919. He served his internship at St. Joseph's Hospital, Chicago, Illinois.

Practically his entire medical career was spent in tuberculosis work. He served as Assistant Medical Director, Oak Forest, Illinois, Tuberculosis Sanitarium, from 1921 to 1927; Medical Director and Superintendent of

Champaign County Tuberculosis Sanitarium, Urbana, Illinois, from 1927 to 1937; and Medical Director of the former Ottawa Tuberculosis Sanitarium, Ottawa, Illinois, until the time of its closure in 1949. Following closure of the sanitarium, he retired because of ill health.

Dr. Bell was quite active in tuberculosis and civic activities throughout the state of Illinois. In addition to being a member of his County, State and American Medical Associations, he was a member of the American College of Chest Physicians, the Illinois Trudeau Society, and the American Trudeau Society. He was a member of Masonic Bodies and the Ottawa Elks and Rotary Clubs.

He is survived by one sister, Mrs. B. V. Barr of Ardmore, Oklahoma, and a brother, Mr. D. D. Bell of Chicago, and two nephews.

Darrell H. Trumpe, Governor for Illinois.

RAPHAEL A. BENDOVE

1893 - 1951

Dr. Raphael A. Bendove was graduated from the Albany, New York Medical College in 1922. He was a specialist certified by the American Board of Internal Medicine; a member of the American College of Chest Physicians; and a member of the American Heart Association. He served on the faculties of the Long Island College of Medicine in Brooklyn, and the New York Postgraduate Medical School and Hospital. He was also on the staff of Sea View Hospital in Staten Island, New York.

Dr. Bendove's life was characterized by deep sincerity and intense devotion to duty. He was most interested in furthering medical education in Israel, and gave much of his time and energies to this cause. He died September 21, 1951, at the age of 58, of acute coronary thrombosis.

Foster Murray, Governor for New York.

ANDREW C. HENSKE

1883 - 1950

Dr. Andrew C. Henske was born in St. Louis, Missouri, December 15, 1883 and died July 9, 1950, in the same city where he had practiced medicine for over 45 years.

Dr. Henske received his degree of Doctor of Medicine at Washington University in 1906. Following his graduation, he interned at City Female Hospital, St. Louis, Missouri in 1906-07. He was appointed Assistant in Internal Medicine on the Staff of Mullanphy Hospital, 1907-08, and physician in charge of the St. Louis Municipal Tuberculosis Clinic, 1910-13. He served as internist at St. Mary's Hospital from 1913-25.

Dr. Henske was diplomat of the Board of Internal Medicine. His subspecialty was Tuberculosis. He was a member of the faculty of St. Louis University School of Medicine where he was Senior Instructor in Internal Medicine and Assistant Professor of Clinical Medicine. He was associate physician at Firmin Desloge Hospital and St. Mary's Group Hospitals, and consultant tuberculosis physician at St. Louis City Sanatorium and St. Louis County Hospital. He was Medical Director of Mount St. Rose Sanatorium, and had served in that capacity for several years. He also served as Medical Director of the Mutual Savings Life Insurance Com-

pany of St. Louis, and as a member of the Selective Service Rehabilitation Board. He was a member of the St. Louis Medical Society, the Missouri Medical Association, American Medical Association, American College of Chest Physicians, and American Trudeau Society.

Dr. Henske was beloved by all who knew him. He distinguished himself not only in his chosen profession, but also as an educator and leader in his specialty.

Charles A. Brasher, Governor for Missouri.

JOHN W. STACEY[1]

1902 - 1951

Dr. John W. Stacey, born November 12, 1902, in Toronto, Canada, died November 11, 1951, of a brain tumor, after a year's illness. Dr. Stacey was educated in Canada, and received his medical degree from the University of Manitoba in 1925. After a short period of practice in North Dakota he moved to Arizona, began practice in Yuma, becoming the leading physician there over a period of years. His first wife developed tuberculosis shortly after their marriage, and finally died of the disease fourteen years later. The devotion of Dr. Stacey to his wife over these many years of invalidism will always remain an inspiration to his many friends and patients. He was increasingly stimulated by the problems of tuberculosis and finally gave up the general practice of medicine to work with Dr. Ralph Matson, a former President of the American College of Chest Physicians. Following this, he moved to Tucson where he eventually became the first in that city to practice chest surgery exclusively. He served in the European Theater during the last war, and later became Chief of the Thoracic Surgery Division at Bruns General Hospital, Santa Fe, New Mexico. After working with Dr. Stephen Dolley for a year, he returned to Tucson to continue an active practice in chest surgery. In 1948, he was married to Miss Maren Sundt who, with their three children, survives.

Dr. Stacey was active in many of the medical problems of Tucson, and served as chest consultant to the U. S. Veterans' Hospital. To him goes the credit for initiating aerosol therapy for pulmonary infections. In addition to Fellowship in the American College of Chest Physicians and the American Medical Association, he was a Fellow of the American College of Surgeons.

A good and loyal friend and a skillful chest surgeon has been lost to Dr. Stacey's community.

Howell Randolph, Governor for Arizona.

WALTER C. REINEKING

1881 - 1951

Dr. Walter C. Reineking died of injuries sustained in an auto accident in Wisconsin on July 12, 1951, at the age of 70.

Dr. Reineking was born in Sheboygen, Wisconsin in 1881, and in 1905 was graduated from the University of Wisconsin with a B.A. degree. He received his M.D. degree from the Marquette University School of Medicine, Milwaukee, Wisconsin, in 1907. He served an interneship at St. Joseph's Hospital in Milwaukee, and from 1908 until 1917 he conducted a private practice. During World War I he served as a First Lieutenant

in the Medical Corps, and following the war, he devoted his entire time to the treatment of tuberculosis.

He served as Assistant Physician at the Wisconsin State Tuberculosis Sanatorium from 1919 to 1921. From 1921 to 1925, he served as Medical Director and Superintendent at the Rockford Municipal Tuberculosis Sanitarium at Rockford, Illinois. The next year he served as physician at the William H. Maybury Sanatorium, Detroit, Michigan, and from 1927 through 1930 he served as Superintendent and Medical Director of Grandview Sanatorium, Ironwood, Michigan. In 1930, Dr. Reineking became Superintendent and Medical Director of the Lakeview Sanatorium, Madison, Wisconsin where he remained until 1942. Following this, he accepted a position at the Louisiana State Sanatorium, Greenwell Springs, Louisiana, and for an eight-month period in 1943, he served as Medical Director of the Alexander County Tuberculosis Sanitarium at Cairo, Illinois. He resigned this position to accept his last position as Medical Director and Superintendent of Oaklawn Sanitarium, Jacksonville, Illinois, where he assumed his duties in January of 1944.

Dr. Reineking was active in his local, State, and National Tuberculosis organizations. At one time, he served as Vice-President of the Illinois Tuberculosis Association and Vice-President of the Mississippi Valley Sanatorium Association. He was a member of the American College of Chest Physicians, the American Trudeau Society and the Chicago Tuberculosis Society. He served on the Staff of the Passavant Memorial Hospital of Jacksonville, Illinois, and was a member of the Jacksonville, Illinois, Rotary Club.

Darrell H. Trumpe, Governor for Illinois.

Book Review

Differential Diagnosis of Chest Diseases by Jacob Jesse Singer, Lea and Febiger, Philadelphia, 1949.

This Book represents a notable addition to the medical literature. It is a concise, methodical, explicit presentation of much valuable information. In the first part of this volume, the salient features of various diagnostic procedures are assayed. They have been selected with sound critical judgment and are offered in the light of the author's broad perspective as a diagnostician. Due emphasis is placed on the practical value of clinical history, laboratory methods, roentgenologic procedures and other adjunct techniques. The book is noteworthy for the presentation of original ideas and observations which have been recognized for their merit by the medical profession for a long time. The inclusion of discussion of the anatomic, etiologic and pathologic aspects of various diseases of the thoracic cage, pleura, mediastinum, diaphragm and the lung, enhances greatly the usefulness of the text. There is a generous supply of illustrative cases, with brief, clear-cut portrayal of their significant features. Pertinent roentgenograms have been carefully selected from the author's vast clinical material. Their precise reproduction deserves particular mention. The style is clear and good. The bibliography which follows each subject is well chosen and it is quite up-to-date. The index has been compiled with meticulous care and serves its purpose well. The book is clearly printed. The authoritative text of this volume qualifies it as an outstanding contribution to modern medical writing. It can be highly recommended as a reliable guide in daily practice.

COLLEGE EVENTS

18th Annual Meeting, American College of Chest Physicians, Congress Hotel, Chicago, Illinois, June 5-8, 1952.

New York Chapter Clinical Meeting, Hotel New Yorker, February 21, 1952.

New Jersey Chapter Meeting, B. S. Pollak Hospital for Chest Diseases, Jersey City, February 26, 1952.

Philadelphia Postgraduate Course, March 24-28, 1952.

Texas Chapter Meeting, Dallas, May 5, 1952.

XII Congress, International Union Against Tuberculosis
II International Congress on Diseases of the Chest
Rio de Janeiro, Brazil, August 24-30, 1952.

Chicago Postgraduate Course, October 6-10, 1952.

New York Postgraduate Course, November 10-15, 1952.

MEDICAL SERVICE BUREAU

The facilities of the Medical Service Bureau of the American College of Chest Physicians are available to all who are interested in seeking positions or obtaining applicants in the field of chest diseases. If you wish to advertise in *Diseases of the Chest*, please write to the Medical Service Bureau, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois, for rates and further information.

POSITIONS AVAILABLE

Resident or staff physician wanted for 100 bed tuberculosis hospital 70 miles from Sun Valley, Idaho. Excellent facilities for medical and surgical treatment of chest diseases. Salary comensurate with training and experience, full maintenance provided. Graduate of American school and eligible for Idaho license required. Position under State Merit System. Please address Box 240A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Medical director wanted for tuberculosis hospital at a salary of $4,820.00 per year and full maintenance. Please address Box 241A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Two residents wanted for 175 bed Ohio tuberculosis hospital approved for residency. Salary $250.00 per month less nominal charge for maintenance. Single physician preferred. One vacancy April 1, 1952. One vacancy June 10, 1952. Please address Box 242A, American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, Ill.

Assistant Medical Director in 225 bed tuberculosis sanatorium. For details please write Jefferson Tuberculosis Sanatorium, 3800 Montgomery Highway, Birmingham 9, Alabama.

POSITIONS WANTED

Thoracic and general surgeon, age 34, has seven years' training, two in thoracic surgery including tuberculosis. Passed Part I Surgery. Available in July. Desires association, partnership, institutional appointment with opportunity for private practice. Please address Box 261B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Physician desires residency in tuberculosis medical service. Hospital or sanatorium. Previous training in tuberculosis. Rotating internship. Please address Box 260B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Physician desires residency in tuberculosis hospital or sanatorium. Experienced. For further information please address Box 257B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

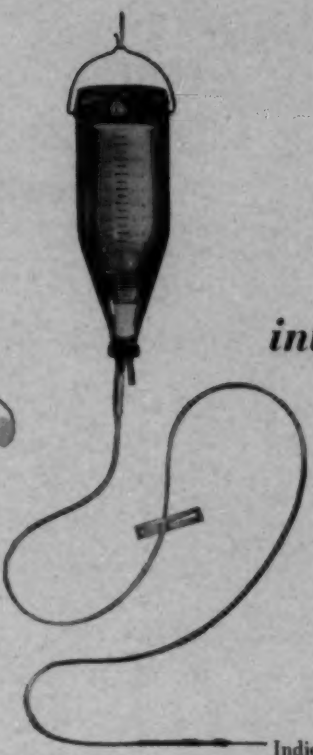
RARE DRUG

A rare drug, so costly that it can only be given away, not sold, was offered to science by Armour and Company in the hope that someone will find out what it does and whether it has any drug value. The new material, a co-enzyme known in laboratory shorthand as TPN and chemically as triphosphopyridinenucleotide, was one of a number of rare biochemicals described in a scientific exhibit shown to the American Association for the Advancement of Science here by the research division of Armour and Company of Chicago. Estimates are that it would cost about $800 a gram, or $363,000 a pound, if there were a pound. TPN is extracted from liver by a complex and difficult process which yields only a few milligrams from a hundred pounds of raw material. Any competent scientist who has some hopeful ideas about it may get some from Armour, while the supply lasts, in quantities of 50 to 100 micrograms—one/20,000th to one/10,000th of a gram. Lawrence L. Lachat, Armour research chemist in charge of the exhibit, said that TPN is a co-enzyme (a substance necessary to permit an enzyme to function in the body). It contains nicotinic acid, the anti-pellagra vitamin, and may be the active form of the vitamin in the body; hence it may be essential to health and to life itself. It was discovered several years ago, but until recently there has never been enough of it for adequate investigation.

USPHS REPORTS

Edward G. McGavran, M.D., M.P.H., dean of the School of Public Health, University of North Carolina, has been appointed chairman of the Board of Editors of the new *Public Health Reports*, according to an announcement made today by Dr. Leonard A. Scheele, Surgeon General of the Public Health Service, Federal Security Agency. The new *Public Health Reports*, the first issue of which will appear this month (January 1952) will be an expanded version of the weekly technical journal of the same name which has been published since 1878 by the Public Health Service, and will include the functions of the monthly Tuberculosis Control Issues of the old *Public Health Reports*.

Terramycin



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Indicated for use in all infections of such severity that intravenous injection is the preferred route, Crystalline Terramycin Hydrochloride Intravenous provides a rapid acting form for the attainment of immediate high serum concentrations. Recommended when oral therapy is not feasible, in severe fulminating or necrotizing infections, in surgical prophylaxis in selected cases, and in peritonitis. For hospital use only.

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	20 cc. vial, 500 mg.

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